DISEASES OF THE BASAL GANGLIA

THEIR RELATION TO DISORDERS OF MOVEMENT

D. DENNY-BROWN
O.B.E., M.D. N.Z., D.Phil. Oxon., LL.D. (hon.), F.R.C.P.
PUTNAM PROFESSOR OF NEUROLOGY,
HARVARD MEDICAL SCHOOL, BOSTON, MASS.

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BEFORE proceeding to physiological analysis it is necessary to define some of the terms employed, and to indicate some general relationships.

One of the most prominent features of diseases of the basal ganglia is *athetosis*. The use of this term is based on its literal meaning of instability of posture, which, in the hand, implies various degrees of swing from a hyperextension of the fingers and thumb, often with pronation of the wrist, to full flexion of fingers (usually trapping the previously flexed thumb), with flexion and usually supination of the wrist. The swings of movement may be only partial when the condition is mild in degree. The hand is almost always involved, the lips, jaw, and tongue more particularly in bilateral cases, and the foot least prominently.

Chorea is a word with many meanings. In the present connection it relates to a continued endless series of movements of the hand and wrist, of the lips, face, and tongue, and of the distal parts of the lower limbs. In their most subtle form the movements are automatic and conflicting reactions to environmental stimuli of all kinds. In more coarse form they become the movements of athetosis, but in choreic movement there is a continual flow of motion without the irregular alternation that characterises athetosis. In choreic movement posture is lost; in athetosis two or more habitual postures can be distinguished.

Rigidity is the common manifestation of parkinsonism. It is essentially a resistance to passively applied motion, distinguished by its plastic quality, presenting a relatively constant resistance throughout the whole range of applied movement. Rigidity is first appreciable in the flexors of wrist and fingers, but as it develops it is felt in both flexors and extensors of both limbs. In most cases of parkinsonism it is a little more prominent in all flexor muscles. Its presence in the face, tongue, and palate can only be inferred from the impedence of small movements in these parts. It is commonly stated that the tendon reflexes are not altered. They are certainly not increased in amplitude in proportion to the degree of resistance to stretch, as they are in spasticity. Electromyographic (E.M.G.) recording shows that a large tendon reflex is present as an electrical response fluctuating in amplitude according to the phase of tremor in which the tendon tap falls.

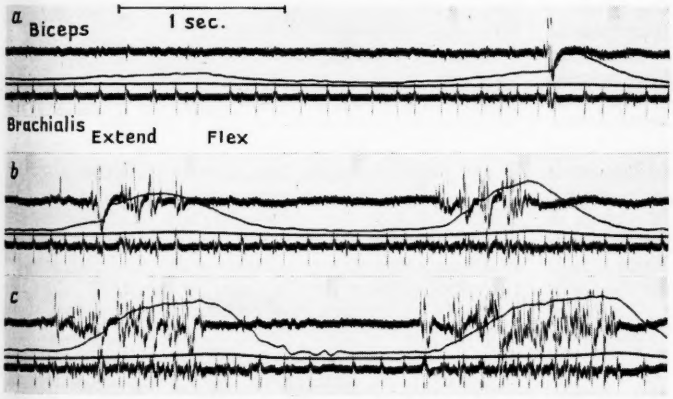

Fig. 8—E.M.G.s of biceps and brachialis anticus, both flexors of elbow, in a patient with paralysis agitans who has been relaxed until rigidity lessened.
In *a* gentle alternating flexion-extension of elbow through about 5° is passively performed. The alternating passive movement is gradually increased in amplitude with each repetition.

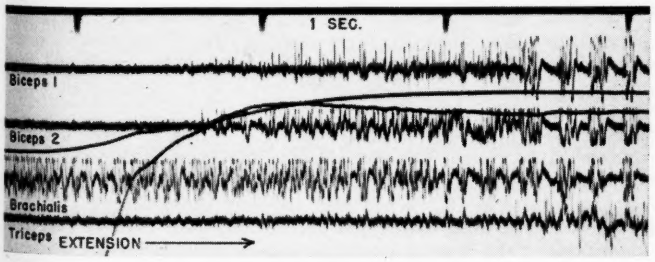

Fig. 9—Paralysis agitans.
E.M.G.s of biceps (2 leads), brachialis anticus, and triceps during gradual passive extension of elbow, to show stretch response and development of tremor.
The two continuous lines indicate the applied movement at the elbow.

As shown previously (Denny-Brown et al. 1953), the plastic rigidity of parkinsonism and its action potentials can be made to disappear if the limb is completely supported, and the patient instructed to relax. Such complete inactivity is easily obtained in arteriosclerotic parkinsonism, less easily in paralysis agitans, and with most difficulty, though occasionally, in postencephalitic parkinsonism. Once the muscles relax completely, with corresponding electrical silence in flexors and extensors, then unimpeded passive movement is possible in either direction at any joint within a small range of 5–10° (the " free interval "). Movement of larger range immediately sets up a contraction in the stretched muscle, whether flexor or extensor (fig. 8), demonstrating that the rigidity is a stretch reflex in each muscle concerned. The " cog-wheel " phenomenon is due to the presence of tremor rhythm, leading to steps of relaxation in the resistance to passive movement. Though common, it is not an essential feature.

The plastic quality of parkinsonian rigidity, that distinguishes it from spasticity, is due to a tendency of motor units recruited into a contraction by stretching, to drop out again one by one as others are recruited. The total number of motor units discharging as the muscle continues

to be stretched, and the corresponding contraction, therefore tend to remain relatively small, giving the plastic quality. When a spastic muscle is stretched more and more motor units respond, and resistance to stretch mounts to a peak. At this point many units suddenly cease responding, and resistance to further stretch melts away (" lengthening reaction "). In plastic rigidity the lengthening reaction affects one motor unit after another from the beginning of stretch, so that resistance to stretch remains approximately constant.

If tremor also complicates the rigidity the appearance and disappearance of units during steadily increasing stretch (after preliminary relaxation) gradually synchronise, until eventually at one point they all cease discharge together and return together. This is the first beat of tremor, and there is commonly a concurrent burst of units in other related muscles at the same joint (fig. 9), then in other previously quiescent muscles in the limb.

Dystonia is a term that has also been used in many senses. I would define it as a fixed or relatively fixed attitude, in association with some other extrapyramidal disorder of movement. In its mildest form it is seen as overextension of the fingers with slight pronation, or as fixity of facial expression (most commonly openmouthed with staring eyes), or continued overinversion of a foot. In greater degree the extremity becomes set in one of the postures of athetosis, with eventual distortion of the lips and tongue, torticollis, or tortipelvis. The muscles concerned in the fixed posture offer an increasing resistance the more the part is moved away from its primary position. In intense dystonia the resistance to attempted passive movement is springy in quality, and the part flies back to its habitual posture when released. In less degree dystonia presents a plastic rigidity with perhaps very slight palpable increase in resistance as the limb is moved away from the dystonic posture. The E.M.G. is indistinguishable from that of parkinsonian rigidity. As dystonia becomes more intense, more and more of the motor units fail to show a lengthening reaction, and they continue to discharge as still more units join the response. Contractile resistance then steadily increases with increasing stretch.

In the dystonias of postencephalitic parkinsonism and of dystonia musculorum deformans different parts of the body are separately involved. The resulting postures are usually asymmetrical and incongruous. I shall refer to this type as *segmental dystonia*.

The mode of onset of abnormal attitudes in Wilson's disease is usually different. Both limbs on one side are affected together. Very gradually slight abnormalities of attitude become more fixed, and the abnormal attitude develops as a whole. It is then seen, as so well described by Wilson (1912), as flexion of both upper limbs, with hyperflexed, slightly pronated wrists, and at first overextended and later overflexed fingers. The lower limbs are extended, and the ankle-joints plantar-flexed and inverted. This condition is usually referred to as the rigidity of Wilson's disease, but by my definition it is dystonia. In the early stages it is a plastic rigidity, but gradually the lengthening reaction is lost. I call it *hemiplegic dystonia* from its general resemblance to the pattern of hemiplegic spasticity, and from its tendency to affect all the parts on one side together.

Finally one must recognise that, particularly as an end stage in paralysis agitans and related states, a persistent attitude of flexion may occur in all limbs—the wrists over-flexed and pronated, the fingers extended, the lower limbs flexed on the abdomen, and the feet stiffly plantar-flexed. In this condition the abnormal attitude tends to develop as a whole. In milder degrees it also has a background of plastic rigidity, with steady neuronal discharge in proportion to the degree of maintenance of the abnormal attitude. I shall refer to it as *generalised flexion dystonia*. It is the pallidal syndrome.

Tremor.—By common usage tremor is a rhythmical alternation in movement at a rate of more than one beat a second. It must be recognised, however, that the disorder may begin with isolated single beats, as in " liver flap". The relation of tremor to movement is only of relative value in distinguishing types of tremor. Whereas parkinsonian tremor is first apparent only in very slight degrees of muscular contraction, as the tremor becomes more intense it is apparent during greater degrees of contraction and in full development may never be absent.

The term *myoclonus* has many different connotations. It is essentially an unpredictable rapid jerk or twitch of one or more muscle groups, distinguished from chorea by its abruptness and brevity. Any muscle group may be involved, but an abrupt flexion of one or more joints in both upper limbs, with extension of the neck, are frequent components. The jerks may at times appear in a rapid series of two or more in succession. Myoclonus of this type is common in extrapyramidal disease. We must omit from this brief account its relation to " palatal " myoclonus, epileptic myoclonus, and other types of bulbar and spinal twitching of similar kind.

Interrelations of the Motor Disorders

Chorea, Athetosis, and Parkinsonian Tremor

Although it is a diagnostic convenience to separate these various types of motor disorder, the first step in gaining a proper understanding of their significance is to seek relationships between them. The model for this whole series seems to me to be the phenomenon of athetosis. If one has in mind the two elementary postures of the fingers and wrist—overextension with pronation and overflexion with supination—between which the movement alternates, one may find the same two postures in post-hemiplegic athetosis and in double athetosis, though the speed of alternation is faster in the latter. The involuntary movements of Huntington's chorea reproduce momentarily the same postures again and again, with many partial variants (Denny-Brown 1950), gradually becoming more stereotyped. In dystonia musculorum deformans one or other posture is found as a fixed attitude (Denny-Brown 1945). In the rapidly progressive type of Wilson's disease the transition from choreic movement to athetosis to dystonic attitude may be observed in the same patient in the course of months. Most commonly the dystonic fixation of the hand in Wilson's disease is with fingers extended, though in time the wrist becomes overflexed (fig. 2). Very rarely a dystonic attitude of overflexion of the fingers is present from the beginning, and the hand ultimately develops a severe dystonic grasp which the patient is unable to relax.

In some unusual variants of Wilson's disease dystonia develops only very slowly, and in such cases a parkinsonian tremor may eventually supervene after months of athetosis. When this happens the athetosis gradually becomes more rapid, and the amplitude of movement less. The fingers, instead of closing over the previously overflexed overadducted thumb, now close only to semiflexion —the adducted thumb also—and at more rapid intervals. Eventually the partial movement, more regularly repeated, becomes the "pill rolling" tremor of parkinsonism,

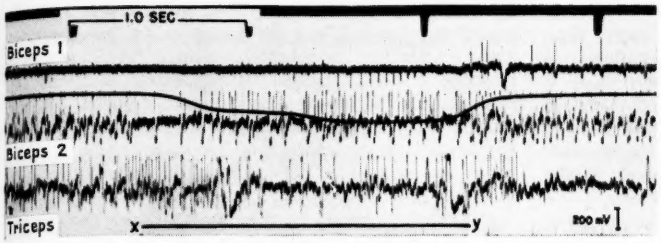

Fig. 10—Arteriosclerotic parkinsonism.
E.M.G.s of biceps (1 and 2) and triceps during flexion (*x*) and extension (*y*) of elbow.

with appropriate opposition of the thumb (Denny-Brown 1950).

Chorea, athetosis, and parkinsonian tremor are also topographically related, for each involves primarily the hand, in next degree the lips and tongue, and in ultimate development the ankles. We therefore regard them as members of a related series of fluctuations of posture with important physiological connotation.

Parkinsonian Rigidity, Dystonia, and Myoclonus

In the more intense plastic rigidity of parkinsonism, particularly in arteriosclerotic types with little tremor, the lengthening and shortening reactions at first become more fully developed. When the elbow is extended there is a burst of discharge in the flexors followed by relaxation to the previous level. The phase of relaxation (lengthening reaction) occurs earlier than in stretch of a spastic muscle, and coincident with it is a contraction in the extensors (shortening reaction) (fig. 10). On flexing the elbow the reverse process readjusts the quantity of contraction to its previous level. Both flexors and extensors show a rapidly adjusting stretch reaction. Later, as dystonia becomes more pronounced, fewer of the motor units exhibit a lengthening reaction in the flexor group in the upper limb, and they continue to discharge as long as stretch is maintained. The extensor group then show correspondingly less shortening reaction. Ultimately, when dystonia is fully developed, all the discharge is directly proportional to length of muscle, and the lengthening and shortening reactions have vanished. This progressive loss of lengthening reaction in the elbow flexors is associated with two other features—(1) the activation of other synergic flexors by stretch of one of them, and (2) increasing numbers of units continuing to discharge at the shortest length of the muscle. Some of these are stimulated by tension on other flexor muscles and they can be got to cease discharge by more complete relaxation. Some are influenced by labyrinth and neck reflexes and can be silenced only by manipulating the head and neck.

At an intermediate stage of development of dystonia of hemiplegic distribution, when many units still show lengthening and shortening reactions, a rapid stretch provokes discharge of a large number of motor units together, dissipating in several beats, during one or more of which bursts in widespread synergist muscles cause the sudden contraction that the clinician calls a " myoclonic jerk ".

These observations, which can readily be repeated while any type of dystonia is developing, indicate that the essential conflict between proprioceptive inhibition and excitation in all these types of rigidity and dystonia is one of degree and not of kind.

Tremor and Rigidity

As already mentioned, in dystonic states the lengthening reaction in one muscle is associated with a shortening reaction in its antagonist. If the plantar flexor of the foot, or palmar flexor of the wrist, is suddenly stretched, the response in the shortened antagonistic extensors is often visible to the eye as a brief contraction of the tendons of corresponding pretibial or wrist dorsiflexors. Fig. 11*a* is an E.M.G. record of this phenomenon, which is generally known as " Westphal's paradoxical reaction " (Westphal 1878), or as the " tonic postural reflex " of the French school (Foix and Thévenard 1923). Like Kinnier Wilson (1925) and others, I have found the sign to be inconstant in paralysis agitans and Wilson's disease, though it is prominent in some cases. A corresponding delayed burst of discharge in the wrist extensors follows 60–70 msec. after a tendon reflex in the finger flexors under these circumstances (fig. 11*b*). Matthews and Rushworth (1957) found that procaine infiltration of the motor point of a muscle selectively paralysed the gamma efferents to the muscle spindles. Two years ago, with Dr. Geoffrey Rushworth I reinvestigated this phenomenon and found that such infiltration of the motor point of a dystonic muscle, whether wrist flexor or post-tibial muscles, abolished the reaction to stretch both in the muscle concerned and in its antagonist, leaving it still possible to innervate either group by will. The reaction is therefore clearly proprioceptive, and it is related to the antagonistic autogenetic reflex excitatory effect of the annulospinal endings versus the inhibitory secondary sensory flower-spray endings of the muscle spindles.

This double effect demonstrates clearly that such plastic states represent the release of two opposing types of stretch reflex. The prominence of the paradoxical reaction in wrist and ankle is related to an intermediate phase of development of dystonia in these groups, so that the sudden stretch falls on muscles that are already contracting. With a lesser degree of dystonia there is no reaction, and in greater dystonia all the response is in the stretched muscle.

When tremor complicates moderate dystonia the first response of the stretched muscle is a prolonged beat of

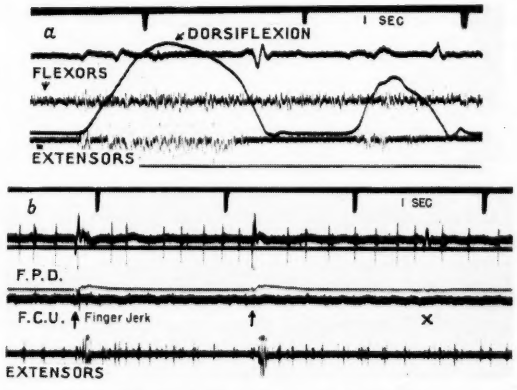

Fig. 11—Arteriosclerotic parkinsonism.
E.M.G.s of flexor profundus digitorum (F.P.D.), flexor carpi ulnaris (F.C.U.), and extensors of wrist, during sudden passive dorsiflexion of wrist (*a*), and during finger jerks (*b*). x represents a subliminal tap on the finger flexors.

tremor, the cessation of which is associated with a similar prolonged beat of tremor in the antagonist. Tremor then appears as a series of alternating primary and paradoxical reactions. A final prolonged burst of tremor when a tremulous muscle is suddenly shortened is the reverse reaction. From this point of view tremor is a rhythmical alternation of the conflict of the same heightened proprioceptive reciprocal effects that are represented in the lengthening and shortening reactions of dystonia.

The observation of Walshe (1929) that parkinsonian rigidity could be abolished by cocainisation of the motor points of a rigid muscle, leaving tremor unaffected, might appear to contradict these conclusions. The explanation lies in the spread of contraction, whether rigidity or tremor, from one muscle to another. The stretch reflex can no longer be elicited in a cocainised muscle, but the paradoxical reaction or tremor from other muscles can still affect it. Total surgical deafferentation of the limb by dorsal-root section, reported by Pollock and Davis (1930), also demonstrates the point, for then only a variable degree of slowly rhythmical neck and labyrinthine reflex remained.

These findings indicate that plastic rigidity, parkinsonian tremor, and dystonia are different aspects of a conflict of released proprioceptive reactions. The conflict is resolved more slowly in plastic rigidity, more rapidly and rhythmically in tremor, and not at all in intense dystonia. To find the reason for these conflicting aspects of release of low-level reflexes we must turn to the question of cortical control of proprioceptive reactions.

The Two Basic Postures of Athetosis

In earlier studies of disorders of movement produced by cortical lesions (Denny-Brown 1958), I have distinguished two general types of disorder:

The first type is represented by the tendency of medial frontal-lobe lesions to facilitate tactile and visually directed palpatory reactions in the hand and lips, of which the instinctive grasping and sucking reactions are the prototypes. The fundamental change in behaviour is more general and comprises all the manifold elements of frontal apraxia, including a stiffening of the whole limb in response to contact (gegenhalten).

The second type is an opposing set of reactions, released by parietal-lobe lesions, characterised by instinctive tactile and visual avoiding responses which determine withdrawal, flexion of the limbs, over-extension of the fingers, and residual stiffening of the limb in this posture (" catatonic persistance of attitude "). Two general areas of cortex, medial frontal and lateral parietal, are organised in this respect, with corresponding visual exploratory and avoiding responses in the posterior-parietal and temporal regions (Denny-Brown 1956, Denny-Brown and Chambers 1958).

These two physiological types of response are behavioural antagonists. In each case a specific type of environmental stimulus " triggers " a proprioceptive reaction in the appropriate muscles, most evident as the proprioceptive component of the grasp reflex.

When the cortical lesion is extensive not only is the corresponding highly developed oriented " instinctive " response to the environmental stimulus lost, and its antagonist reaction facilitated, but a subcortical representative of the lost reaction also makes its appearance. The subcortical response is a simpler reaction no longer, oriented to the source of stimulus, and it requires a more coarse stimulus. Thus the grasp reflex, a subcortical response, replaces the delicately oriented "instinctive grasp response". In common with released reactions the response now requires a heavy contact stimulus, involves more muscles, and persists longer after the stimulus. The corresponding proprioceptive response becomes more prominent and more persistent. All further attempt to move the limb is impeded for a time after any contact with the palm of the hand. In some cases not only the arm but also the leg on the same side stiffens in response to any coarse contact with the hand. This is the disorder called " tonic innervation " by Wilson and Walshe (1914). Similarly, with large posterior-cortical lesions, a moving stimulus in the " hemianopic " visual field induces an eye movement which the patient cannot make voluntarily, and the deviation of eyes and head, once elicited, lasts a long time. This is tonic innervation of the eyes and head.

Tonic innervation of this kind is the reason for persistence of abnormal attitudes as a result of purely cortical lesions. The pattern of extended fingers in an extensive parietal-lobe lesion, for example, is identical with that seen in athetosis, and it can be called " athetoid ". It is not athetosis as we have defined it, for there is no essential

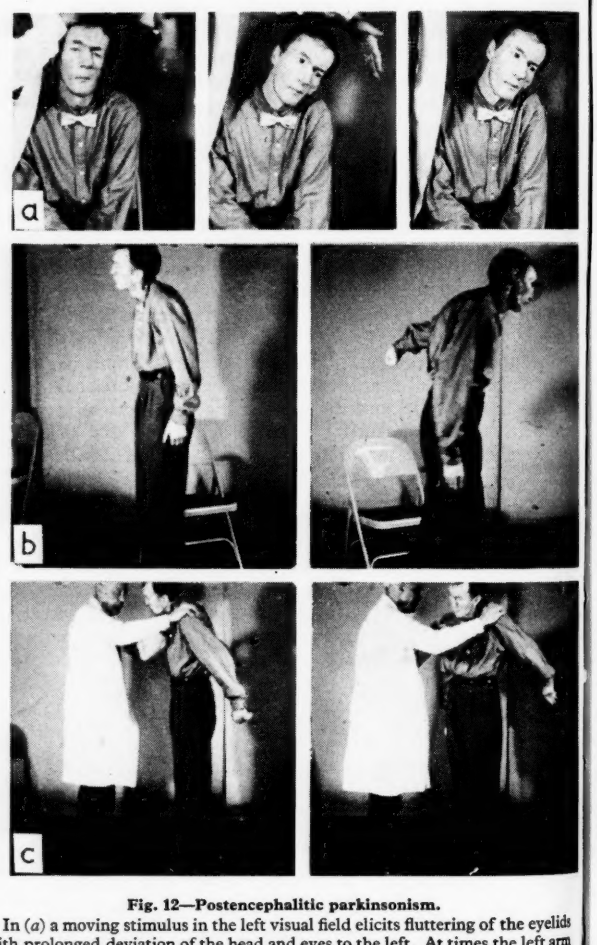

Fig. 12—Postencephalitic parkinsonism.

In (*a*) a moving stimulus in the left visual field elicits fluttering of the eyelids with prolonged deviation of the head and eyes to the left. At times the left arm became retracted and abducted during walking (*b*). This posture appeared with passive rotation of the patient to the left (*c*).

conflict, and the attitude is transitory and unidirectional (overextended in parietal lesions, overflexed in frontal lesions).

The distinguishing feature of true athetosis is that two opposing reactions to the same general type are released together. Thus, in the athetotic hand, a heavy moving contact stimulus with the centre of the palm induces a coarse type of grasp reflex, and a similar contact with the dorsum of the fingers induces an extension of the fingers and wrist (Denny-Brown 1950, 1958). A heavy contact with the sole of the foot leads to a tonic foot response, and a light moving contact applied distally on the sole of the foot causes an extension of the toes with fanning. A combination of such stimuli reproduces the same alternating swings of movement in foot or hand that occur spontaneously as athetosis in the same patient. Their long persisting tonic proprioceptive after action heightens the existing rigidity to determine the corresponding dystonic attitude. In most types of athetosis the reactions in the hand are biased in favour of avoiding, and those in the foot in favour of grasping. This pattern is that of the underlying hemiplegic dystonia. Coincident with the release of facilitated grasping and avoiding reactions, the muscles activated by these reactions are found to exhibit plastic stretch responses. The condition that has determined release of coarse contact responses has also led to oversensitivity of the proprioceptive reactions normally triggered by contact stimulation. The conflict of stretch reactions represented by plastic rigidity parallels the antagonistic contact reactions.

In the rigidity and tremor of parkinsonism the same factors are operative, for a distally moving contact stimulus in the palm of the hand prolongs the flexion phase, and on the dorsum of the fingers it lengthens the extensor phase, of tremor. In many cases of arteriosclerotic parkinsonism without tremor a double stimulation of both dorsum and palm of the hand by a distally moving contact with the examiner's hands will induce 3–20 beats of typical parkinsonian tremor.

Patients with postencephalitic dystonic states often show the phenomenon of " oculogyric crisis ". In such a patient, instructed to look forward, a coarse moving stimulus in the sensitive visual field (as in fig. 12*a*, where the upper left field is sensitive) may induce a slow tonic deviation of the eyes towards the stimulus, followed by persistent tonic innervation of gaze in that direction for a half to two minutes, associated with the fluttering tonic closure of the lids, typical of spontaneous oculogyric crises. It was also noted that at times this patient walked with the left arm stiffly extended behind him, and the hand tightly clenched (fig. 12*b*). At other times the left arm was semiflexed in front of him, with parkinsonian tremor. The adequate stimulus for this abnormal extension of the arm was rotation of the head (or whole patient) to the left (but not to the right). The change in arm posture associated with passive rotation to the left is shown in fig. 12*c*. This extended retracted posture of the arm for long periods also occurs in other types of segmental dystonia affecting the arm, causing it to be strongly flexed when lying supine, and gradually overextended and retracted when the patient stands or leans forward with the face downward. The operative stimulus with long-lasting effect is labyrinthine.

Coinnervation of antagonists during attempted voluntary movement in athetosis and chorea was thought by Wilson (1925) to represent the primary disorder of motor function in these states. Our investigation indicates that each such spasm is an exaggeration and conflict of the normal reflex factors essential for all movement. If it is agreed that projected tactile and visual grasping and avoiding reactions are an essential substrate for all projected movements of the upper limb, and as such are the basis of learned purposive movements of the hand in the infant, this special difficulty with " willed " or " voluntary " movement disappears.

Some further understanding of the fundamental physiological factors that are in conflict is to be gained from animal experiments.

Lesions of the Basal Ganglia in the Monkey

It is possible to produce bilateral electrolytic lesions up to 3 mm. in diameter in the caudate nucleus, putamen, or globus pallidus of the monkey, without any obvious effect on behaviour. We have ourselves, in Boston, confirmed in this way the observations of Ranson and Berry (1941), Kennard and Fulton (1942), and Laursen (1955). In this respect the observation of Carpenter et al. (1950) regarding the necessity for destruction of at least 20% of the volume of the subthalamic nucleus to produce symptoms evidently holds for these other structures.

Caudate Nucleus

Bilateral destruction of the caudate nucleus in the monkey, produced by suction through a small incision in the prefrontal region just rostral to area 8, resulted in a remarkable change in behaviour. From the first recovery from anæsthesia the animal showed restless pacing movement up and down the back wall of the cage, facing the wall, whenever the examiner entered the room. Within a few hours this behaviour alternated with a few steps to the left side of the front of the cage to look out, then to the back wall, then again to the front of the cage, and so forth six or eight times, and then there was renewed pacing up and down facing the back wall. This type of restlessness continued day by day. On the third postoperative day it was observed that, if the examiner put a hand or other object on or near the door, the animal turned immediately and jumped at the object, and then jumped back to the back of the cage and continued pacing as before. In the following twelve weeks the pacing to the door gradually became transformed into a circling of the cage, always pausing momentarily at the same place near the door, sometimes pausing once to pace the back wall but often only pausing to look at the wall. If the monkey was excited the full automatisms were repeated in the form they first appeared. Except for these abnormal movements there was no change in reflexes, though it was difficult to obtain instinctive grasping or avoiding responses in the mouth, hands, or feet.

Hyperactivity following destruction of the caudate nucleus has been viewed (Mettler 1942) as equivalent to that which follows bilateral frontal ablation. There is, however, an important distinction. In earlier work we found that hyperactivity after frontal-lobe ablation was determined by compulsive touching. The animal with hyperactivity after bilateral caudate lesions was entirely different. It too conducted a compulsive behavioural promenade, but this was related entirely to the presence of others—usually the observer and, to a less degree, a strange monkey. It had no tactile compulsions, but instead it showed a number of visual compulsions of which visual challenge, visual avoiding, and compulsive visual investigation were the most obvious. It follows that the caudate nucleus must normally be concerned in the integrative balance of responses to environmental contact stimuli with those of visual context.

Putamen

Richter and Klüver (1944) report an observation for thirty hours of a monkey in which necrosis in the caudate nucleus and putamen of both sides had occurred after a lengthy convulsive state. The animal presented a " thalamic " posture when lying on its side, with flexion of the uppermost limbs and extension

of the undermost, and both upper extremities and digits were strongly flexed in other positions. Neck reflexes were present.

It is most difficult to place large lesions limited to the putamen. In our experiments in Boston we have succeeded in placing electrolytic lesions 4 mm. in diameter bilaterally in the rostral putamen, together with 2 mm. lesions in the middle of the putamen, in 2 monkeys. The animals thereafter always stood in a stiff attitude, but when examined in a chair they showed only a soft yielding rigidity in all limbs, without consistent abnormality of posture. When suspended in space by grasping the body all the limbs stiffened, the upper in flexion and the lower in extension. In walking the feet were frequently misplaced. The tactile placing reaction, by which the blindfolded animal reaches out to explore a contact with hand, foot, or lip, was performed very poorly. Visual placing was well performed in all limbs. The grasp reflex was very intense in both hands, but instinctive oriented grasping was absent. There was a marked avoiding response in both feet. Hopping and optokinetic responses were brisk, and labyrinthine postures were very active when the animal was suspended. We conclude, therefore, that the body of the putamen is concerned in contactual reactions, and that when these are impaired more general labyrinthine and body-contact reactions are released.

Fig. 13—Bilateral lesion of inner globus pallidus in monkey.
To show (*a*) the flexion dystonia, and (*b*) failure of righting in a free fall.

Globus Pallidus

Electrolytic lesions of the globus pallidus, successfully placed so as to destroy most of the efferent pathway, had a most remarkable result in 3 of our monkeys. Immediately after recovery from anæsthesia 2 monkeys were unable to stand, and they lay in a posture of general flexion. The hands and feet were quite useless for the first three to five days, being held with elbows, knees, and wrists flexed, ankles dorsiflexed, and the fingers and toes flexed. The mouth was tightly shut, and the jaws were clenched. Any attempt to extend the limbs while the animal was lying encountered a resistance that caused the limb to fly back to the original posture when released (fig. 13*a*). There was failure of effective righting except for an intensification of flexion of all limbs when the body lay in contact with a surface. When raised in air the monkey extended the fingers and toes a little, with a series of myoclonic jerks in the flexors of the upper limbs and extensors of the neck. Any contact with the lips caused the mouth and jaw to be closed tightly. Food introduced into the mouth by tube was swallowed, but the face was expressionless, and the eyes, though open, appeared to fix on the examiner only with difficulty. The resemblance of this posture to that observed in cases of carbon-monoxide poisoning is remarkable.

During survival periods of seventeen and twenty-one days the animals learned to walk. It was then apparent, that though gait was relatively normal in rhythm, the feet were often turned over and poorly placed, and the limbs were overflexed. There was complete absence of both visual and tactile placing, and of tactile grasping and avoiding in both hands and both feet. The hands were not used to bring food to the mouth. There remained a failure of normal sequence of righting reflexes from the reclining posture. After the first week the animal learned to right itself by a convulsive jerk, and then it stood in a stiff attitude, from which it fell easily. If dropped in air upside down, it failed to right itself during the fall (fig. 13*b*). When the monkey met an obstacle, particularly when walking into a corner, the head would be lowered and the neck flexed until the top of the head rested on the floor. The animal would remain in this peculiar attitude for as long as five minutes. This was traced to weakness of body-righting reflex, acting on the head.

The lesions were incomplete, having destroyed about half of the inner globus pallidus, part of the related frontopontine tract, and all the ansa lenticularis and lenticular fasciculus. In other animals it was found that, if any of the efferent pathway escaped destruction, the effect was very slight.

The peculiar behaviour and postures of an animal with an inner globus-pallidus lesion was in this way traced to loss of all placing reactions, labyrinthine righting reactions, and optic righting reactions, in association with a very intense tonic body-contact response, leading to flexion of limbs and of both hands when the body made broad contact with a surface. Another animal with lesions that on one side damaged the outer globus pallidus, and on the other severed the outer ansa lenticularis, presented a hemiplegic dystonia when lying, with extension of all limbs when suspended in air (fig. 14). Placing and grasping were absent. Labyrinthine reactions were overactive, and it could right itself slowly when falling blindfolded in space. This indicates that the bundles of nerve-fibres entering the globus pallidus from the thalamus must serve the labyrinthine righting-reflex function that was absent in the first animals.

After making these observations we found that Richter (1945) had reported the production of symmetrical necrosis of the globus pallidus in monkeys by exposure to carbon-disulphide gas. His monkeys presented many of the postures described above, with marked intention tremor in addition. There was plastic rigidity of the limbs. Tonic neck reflexes could not be obtained, and the animal was unable to eat. The necrosis of the globus pallidus was extensive. In 2 of 5 animals the substantia nigra was cavitated, but this did not alter the syndrome. Milder changes were found in the subthalamic and dentate nuclei, and in one animal in the hypothalamus. Our own

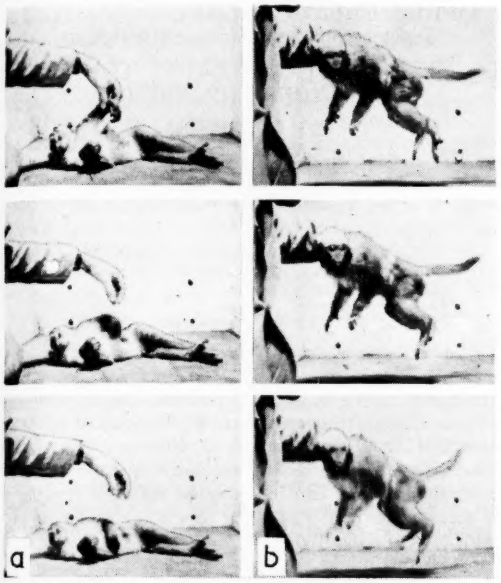

Fig. 14—Bilateral lesion of the outer globus pallidus in the monkey. To show (*a*) hemiplegic dystonia, and (*b*) extension of limbs when suspended in space.

experiments show that, except for intention tremor, the globus-pallidus lesion can alone reproduce the syndrome.

Substantia Nigra

Experimental production of bilateral lesions in the substantia nigra in the monkey has not been associated with rigidity or tremor (Ranson, cited by Cannon et al. 1944, Carrea and Mettler 1955). von Economo (1902) found that disorders of mastication and swallowing resulting from experimental cortical lesions were associated with degeneration of this nucleus. He later (von Economo 1931) related the yawning and masticatory tics of acute lethargic encephalitis to destruction of the substantia nigra. Inability to chew was noted by Carrea and Mettler in a monkey with bilateral nigral lesion.

From the studies of Magnus (1924) and Rademaker (1926), it was determined that the rabbit and cat exhibit tonic neck and labyrinthine righting reflexes, and body-righting reflexes acting on the head, after section of the brain-stem just in front of the midbrain. In the midbrain monkey such righting effects are very weak, there being no effective righting. The decorticate (thalamic) monkey exhibits tonic body-on-body and labyrinthine righting reflexes, but still does not rise and stand, or show optic righting. The effects of globus-pallidus lesions described here indicate that, for labyrinthine righting to be effective in the monkey, the presence of a thalamopallidal connection is necessary. Subthalamic structures mediate body-on-body (contact) responses. Lesions of the outer globus pallidus leave both labyrinthine and body-righting reflexes intensely overactive in the form of enhanced proprioceptive reactions (rigidity). Facile righting requires the presence of intact putamen in addition to thalamus and globus pallidus. The evidence gained from the effects of partial lesions of putamen in monkey and man indicates that this structure is necessary for the elaboration of fragments of contact righting reactions into contactual exploratory and avoiding responses, and of labyrinthine effects into optic reactions.

Conclusions

A survey of the natural history of diseases affecting the basal ganglia led to the conclusion that the involuntary movements they cause are intermediate stages in a disintegration of motor function, each leading to a disorder of postural attitude when complete. A progressive rigidity, at first plastic in quality, but gradually becoming more resistant to passive manipulation, accompanies the process of dissolution. The reflex effects that modify these movements and attitudes show that the whole basal-ganglionic system is necessary for the regulation of movement by environmental factors. The highly differentiated pyramidal tract is ineffective without the extrapyramidal system.

Lesions of the caudate nucleus release a profusion of cortical automatisms (chorea), suggesting that this structure is concerned in suppressing one group of cortical reactions while another is active. Thus damage to the head of the caudate nucleus releases visually determined automatic behaviour, and lesions of the tail of this nucleus may be expected to release tactile automatisms.

The involuntary movements that result from diffuse partial lesions of the putamen and globus pallidus are found to be different aspects of incomplete control of labyrinthine and body-righting reflexes, and the cortical mechanisms that normally suppress and modify them. All these reactions exemplify the principle that for every cerebral cortical function that is lost a corresponding coarser type of subcortical reaction is released. The adequate stimulus is then not so specific, and the reaction involves more body parts, long outlasting the stimulus. Thus such movements as prehension and visual fixation become tonic innervation of grasp and tonic deviation of the head and eyes respectively, after appropriate extensive cortical lesions.

The effect of lesions of the putamen is to release tonic grasping and tonic avoiding together, resulting in the distortion of movement called athetosis, often with conflict of corresponding visual responses. The more severe these disorders become the more the release of the substratum of labyrinthine and contact-righting responses is evident. The attitude of body parts then becomes gradually more fixed in the pattern of overactive righting reflexes characteristic of the decorticate primates (hemiplegic dystonia). Lesions of the outer putamen produce such disorder in only one limb or body part (segmental dystonia).

Lesions of the globus pallidus result in a remarkable paucity of movement, including speech, reflecting a greater loss of the reflex as well as cortical facilitatory factors that are essential to all types of movement. The posture of flexion of all limbs that results is greatly intensified by pressure contact with a broad body surface, but shows little if any labyrinthine response. I have presented evidence that the usual lesions of parkinsonism are such as to damage the fibre systems of the globus pallidus. There is great variation in the symptomatology, depending not only on the intensity of the lesion but also on the degree to which thalamopallidal fibres are spared. Our investigation indicates that the more rigid elements of dystonia result from the thalamic labyrinthine reactions. The tremor of parkinsonism shows the same conflict between grasping (exploratory) and avoiding reactions that underlie athetosis, but in more rhythmically unstable form. Flexor myoclonus is an even more unstable manifestation. The effect of surgically induced lesions of the thalamus in lessening or reducing both tremor and rigidity in some cases (Cooper and Bravo 1958) indicates that overaction of the thalamic reflex circuit is an important factor in this type of instability.

Both clinical neurological study and experimental evidence indicate that the globus pallidus is an extremely important structure for integration of movement. It is

indeed the "head ganglion" of the motor system of primates. Though small surgically induced lesions may have remarkable effects in lessening conflicts of physiological factors in movement, I should warn that I have twice observed the mute akinetic pallidal syndrome to have resulted from surgical destruction of this region in man. The milder effects in other cases do not prove that a lesion of the globus pallidus "is no longer acceptable" as an explanation of parkinsonism (Jung and Hassler 1960).

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LIPID AND FATTY-ACID COMPOSITION OF CORONARY AND CEREBRAL ARTERIES AT DIFFERENT STAGES OF ATHEROSCLEROSIS

C. J. F. BÖTTCHER
D.Sc. Leiden
PROFESSOR OF PHYSICAL CHEMISTRY

E. BOELSMA-VAN HOUTE
Ph.D. Leiden

C. Ch. TER HAAR ROMENY-WACHTER
M.D. Leiden

F. P. WOODFORD
M.A. Oxon., Ph.D. Leeds

C. M. VAN GENT
Ph.D. Leiden

From the Physical Chemistry Laboratory, University of Leiden, The Netherlands

IN a previous paper, we (Böttcher et al. 1960) presented analyses of lipid fractions and of their fatty acids in human aortic tissue at different stages of atherosclerosis. It has generally been assumed that both the lipid composition of the smaller arteries and its variation with the severity of the disease are similar to those in the aorta. Some preliminary results (Böttcher et al. 1959b) indicated, however, that this might not be so, and that the aorta might not be a satisfactory model for the study of atherosclerosis in those smaller arteries where the presence of atheromatous lesions more often leads to serious dysfunction. We now present more extensive figures for the lipid and fatty-acid composition in coronary arteries and in the circle of Willis.

Few previous studies of lipid composition in these arteries have been undertaken. That of Lundbaek and Petersen (1953) was confined to highly diseased coronary arteries, and set out to establish whether there were differences between these arteries in diabetic and non-diabetic subjects. In the work of Buck et al. (1954), lipids from cerebral arteries at various stages of atherosclerosis were examined. In neither of these investigations were the lipid fractions isolated for detailed examination. Lewis (1958) examined the fatty-acid composition of the cholesterol esters of four atheromatous coronary arteries, and concluded that they were highly saturated compared with those of plasma.

Methods

The preparation of the small arteries had to be carried out differently from that of the aorta. Handling was more difficult and the tissues had to be prevented from drying out during the procedure.

The coronary arteries were dissected from the heart as close to the apex as possible, laid out topographically on cotton-wool soaked in physiological salt solution, and stored at 2°C in a closed petri dish for 12 to 24 hours. The arteries were then cut open and the degree of atherosclerosis was established and recorded (see fig. 1 of Classification of Atherosclerotic Lesions, W.H.O. 1958). Under a dissection microscope (magnification of ×10 to ×16), a cut was made with a sharp scalpel or an injection needle through the intima into the media, stopping

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short of the external elastic membrane. The raw edge of the cut was grasped with a pair of forceps, and the intima, together with most of the media, was easily peeled off from the adventitia.

The circle of Willis offers special difficulties: the brain arteries are even smaller and have a thinner wall than the coronary arteries. It is not essential to remove the adventitia, which is very thin, and appears on histochemical examination to contain no lipids. The arteries were rinsed in a physiological salt solution to clean them from adherent blood and clots, held tenaciously in the narrow lumen. The arteries were transparent in the isotonic salt solution, and the degree of atherosclerosis could therefore easily be defined and recorded (fig. 3 of W.H.O. 1958).

The aortas in the previous investigation were divided into four groups according to the degree of atherosclerosis:

Stage 0: no atherosclerotic lesions discernible at a magnification of × 10.

Stage I: fatty streaks and/or spots present.

Stage II: fibrous plaques and/or atheromas present.

Stage III: lesions as above, with additional complications—e.g., ulceration, necrosis, hæmorrhage, thrombosis.

The coronary and brain arteries were divided into two groups: 0/I (undiseased or hardly diseased) and II/III (severely diseased), corresponding to combinations of the stages as defined for aorta. Since the analysis of variance of the percentage composition of aortic lipids and of the fatty-acid percentage of the aortic cholesterol esters and glycerides showed a high level of significance only for the differences between the stages 0 and I on the one hand, and the stages II and III on the other

TABLE I—COMPOSITION OF LIPIDS FROM CORONARY-ARTERY PREPARATIONS AT DIFFERENT STAGES OF ATHEROSCLEROSIS

—	Stage of disease	
	0/I	II/III
Number of samples	10	14
Average age (years)	20	47
Average weight of lipids analysed (mg.) per sample	30	63
Lipids as percentage of dry tissue (mean)	20·6	22·3
Mean percentage composition of lipids:		
Phospholipids	28·4	32·1
Free fatty acids	6·7	4·9
Free cholesterol	6·1	11·9
Cholesterol esters	8·8	24·6
Triglycerides	49·7	26·6
Percentage phosphorus in phospholipid fraction (mean)	1·62	2·06

(Böttcher et al. 1960), a comparison of the groups 0/I and II/III should reveal most of the important trends in the course of the disease.

No material was used from persons who had been suffering from diseases known to be associated with gross disturbances of lipid metabolism. An exception was made for a circle of Willis from a diabetic patient, which was the only severely diseased circle we have met with. In the specimens we have examined, the brain arteries were not affected to the same extent as were the aorta and coronary arteries. As table III shows, the average age of stage 0/I of the circle of Willis is much higher than the corresponding figure for the aorta and the coronary arteries.

It was possible in only a few stage II/III cases to analyse lipids from the arteries of single individuals. Most of these small arteries yielded no more than a few milligrammes of lipids, and the stage 0/I "samples" referred to in tables IV to VII are actually pooled lipids from up to five coronary or brain arteries. For stage II/III, two arteries usually yielded the required amount (at least 20–30 mg.) of lipids. The arteries were stored, until the arrival of complementary material, in the freeze-dried state under methanol-chloroform at −25°C.

Methods of analysis of the lipids were as previously described (Böttcher et al. 1959a, 1960). The prepared material was freeze-dried and extracted with methanol/chloroform (1/2), and the extract purified over a column of powdered cellulose. The lipids were divided into phospholipids, free fatty acids, cholesterol esters, and glycerides plus free sterols. The fatty-acid mixtures obtained from the four fractions were methylated and their compositions determined by gas/liquid chromatography over polar (maleic acid/adipic acid/ethylene glycol polyester) and non-polar (Apiezon L) stationary phases.

TABLE II—COMPOSITION OF LIPIDS FROM BRAIN-ARTERY (CIRCLE OF WILLIS) PREPARATIONS AT DIFFERENT STAGES OF ATHEROSCLEROSIS

—	Stage of disease	
	0/I	II/III
Number of samples	8	9
Average age (years)	48	63
Average weight of lipids analysed (mg.) per sample	21	52
Lipids as percentage of dry tissue (mean)	16·1	20·0
Mean percentage composition of lipids:		
Phospholipids	58·2	37·5
Free fatty acids	5·7	4·1
Free cholesterol	9·3	14·7
Cholesterol esters	7·5	28·1
Triglycerides	20·0	16·0
Percentage phosphorus in phospholipid fraction (mean)	2·17	2·41

Statistical evaluation of the results was not considered necessary. The major differences noted were all so large compared with the range of values in each group that they were undoubtedly of significance. Furthermore, most of these differences between 0/I and II/III arteries are in the same sense as those observed for aortas. Where this is not the case, and where the differences are comparable with the individual variation, this fact is noted in the text. These latter results should be regarded as preliminary indications of trends that have to be more fully examined.

Results

The Lipid Composition

The mean lipid compositions of the stages 0/I and II/III of the coronary arteries are presented in table I, and of the brain arteries in table II. A comparison between coronary arteries, brain arteries, and aortas is given in table III.

The percentage of lipids in coronary and brain artery tissue is much higher than in the aorta, both in the undiseased and atherosclerotic stages. Whereas there is a threefold increase (from 3·6% to 10·9%) from stage 0/I to stage II/III in the aorta (Böttcher et al. 1960)—an increase which has been noted as the most characteristic feature of aortic atherosclerosis by many earlier workers—the smaller arteries have initially about five times as much lipid as the aorta and this percentage increases by a comparatively small amount with increasing severity of the disease. The final value is, however, highest in the coronary arteries and lowest in the aorta. These figures show a wide variation from sample to sample, and too great reliance should not be placed on them as a basis for biochemical interpretations. The *composition* of the lipids obtained is, however, much more constant within each group (0/I or II/III).

TABLE III—COMPARISON OF PERCENTAGE LIPID COMPOSITION IN DIFFERENT ARTERIES

—	Aorta		Coronary arteries		Circle of Willis	
	Stage 0/I	Stage II/III	Stage 0/I	Stage II/III	Stage 0/I	Stage II/III
Average age (years)	18	57	20	47	48	68
Phospholipids	58·0	33·5	28·4	32·1	58·2	37·5
Free fatty acids	8·0	2·0	6·7	4·9	5·7	4·1
Free cholesterol	10·1	19·4	6·1	11·9	9·3	14·7
Cholesterol esters	8·8	36·1	8·8	24·6	7·5	28·1
Triglycerides	15·0	10·6	49·7	26·6	20·0	16·0
Percentage of phosphorus in phospholipids	2·67	2·74	1·62	2·06	2·17	2·41

A striking characteristic of the lipids from the coronary arteries is the high percentage of triglycerides, which predominate over all other lipid fractions—even over sterol esters in stage II/III, in spite of the higher percentage of the latter in the more severely diseased arteries. The percentages of phospholipids and of free fatty acids are not significantly different at the two stages.

In the circle of Willis, the lipid composition and the changes of lipid composition show the same patterns as in the aorta, except that the fall in the percentage of free fatty acids is less marked. These results are in good agreement with those of Buck et al. (1954), who found that when the lipid contents are expressed as weight percentages of the cerebral artery tissue, the only differences which correlate with the disease are those in free

TABLE IV—CHOLESTEROL ESTERS OF DIFFERENT ARTERIES. CHANGES IN MEAN PERCENTAGES OF INDIVIDUAL ACIDS AND COMBINATIONS OF ACIDS WITH ATHEROSCLEROSIS

—	Aorta		Coronary arteries		Circle of Willis	
	Stage O/I	Stage II/III	Stage O/I	Stage II/III	Stage O/I	Stage II/III
Number of samples	12	11	3	5	3	5
Myristic (14:0)	1·8	1·3	3·6	2·0	3·0	1·5
Palmitic (16:0)	18·8	13·5	18·6	15·3	19·5	14·0
Palmitoleic (16:1)	7·1	5·4	11·0	6·6	11·9	8·0
Stearic (18:0)	4·7	1·8	5·5	2·3	4·9	3·0
Oleic (18:1)	31·0	29·3	27·5	29·7	24·1	36·4
Linoleic (18:2)	27·3	36·5	18·2	33·6	19·1	25·5
Eicosatrienoic (20:3)	1·9	2·6	0·9	1·5	1·0	1·9
Arachidonic (20:4)	2·4	4·9	2·3	2·5	1·8	3·0
Saturated	27·1	17·9	33·1	22·2	34·4	20·5
Monounsaturated	39·8	35·8	43·8	38·5	40·7	47·1
Polyunsaturated	33·1	46·3	23·1	39·3	24·9	32·4

cholesterol, cholesterol esters, and the percentage of total cholesterol which is esterified.

The changes in the percentages of the lipid fractions with increasing atherosclerosis therefore show the same trends in all three types of artery (except that the phospholipid percentage does not fall in the coronary arteries).

In order to facilitate comparison of results with those of other authors, the mean percentage of phosphorus in the phospholipid fraction has been added to tables I, II, and III. Most authors base their phospholipid percentage on an estimated phosphorus content, multiplied by a factor (25 or 26) which is based on a supposed average phosphorus content of 4% in the phospholipids. Our phospholipids are determined gravimetrically and the phosphorus content is always much lower than 4%. It is our belief that phospholipids of low phosphorus content (lipopeptides) form an essential part of the mixture and should not be neglected. For comparison of cholesterol/phospholipid

TABLE V—GLYCERIDES OF DIFFERENT ARTERIES. CHANGES IN MEAN PERCENTAGES OF INDIVIDUAL ACIDS AND COMBINATIONS OF ACIDS WITH ATHEROSCLEROSIS

—	Aorta		Coronary arteries		Circle of Willis	
	Stage O/I	Stage II/III	Stage O/I	Stage II/III	Stage O/I	Stage II/III
Number of samples	12	11	3	4	4	5
Myristic (14:0)	3·6	3·1	3·4	2·9	4·2	2·8
Palmitic (16:0)	25·4	22·3	21·2	23·3	27·2	21·8
Palmitoleic (16:1)	5·4	5·7	6·8	6·7	7·0	6·5
Stearic (18:0)	11·4	7·3	6·0	5·3	10·3	7·2
Oleic (18:1)	33·2	37·8	46·5	41·8	27·0	33·8
Linoleic (18:2)	10·1	11·7	7·8	10·1	8·4	11·2
Eicosatrienoic (20:3)	0·7	1·1	0·3	0·5	0·3	1·2
Arachidonic (20:4)	2·7	3·4	0·4	1·7	1·9	3·6
Saturated	43·8	35·0	34·2	34·0	48·3	35·5
Monounsaturated	41·1	45·6	56·6	50·8	38·3	43·5
Polyunsaturated	15·1	19·4	9·2	15·2	13·4	21·0

TABLE VI—FREE FATTY ACIDS OF DIFFERENT ARTERIES. CHANGES IN MEAN PERCENTAGES OF INDIVIDUAL ACIDS AND COMBINATIONS OF ACIDS WITH ATHEROSCLEROSIS

—	Aorta		Coronary arteries		Circle of Willis	
	Stage O/I	Stage II/III	Stage O/I	Stage II/III	Stage O/I	Stage II/III
Number of samples	12	10	3	4	3	5
Myristic (14:0)	2·4	1·8	1·3	2·3	1·9	2·0
Palmitic (16:0)	20·1	17·9	14·8	20·7	19·7	16·0
Palmitoleic (16:1)	3·4	3·9	4·5	4·4	3·5	3·9
Stearic (18:0)	17·4	15·2	12·3	13·3	13·7	11·1
Oleic (18:1)	23·0	23·2	28·4	23·6	24·1	32·3
Linoleic (18:2)	18·2	17·5	27·3	26·2	27·3	22·5
Eicosatrienoic (20:3)	0·9	1·8	0·1	0·1	0·3	0·6
Arachidonic (20:4)	6·8	10·8	0·5	0·2	0·8	2·0
Saturated	43·2	37·3	32·3	39·6	39·2	33·5
Monounsaturated	27·8	28·7	36·9	30·1	30·0	38·6
Polyunsaturated	29·0	34·0	30·8	30·3	30·8	27·9

ratios, &c., allowance can be made for this difference in method by means of the percentages quoted.

The Fatty-acid Composition

To save space, tables showing the complete fatty-acid compositions of fatty acids from all lipid fractions are not given.* The acids found were the same as those shown for aorta lipids in table II of Böttcher et al. (1960).

In table IV to VII comparisons have been made between the aorta, coronary arteries, and the circle of Willis with respect to the fatty acids occurring to the extent of more than 2% of the total, and to the sums of the percentages of saturated, monounsaturated, and polyunsaturated acids from each lipid fraction. It can be seen that each lipid type has its characteristic fatty-acid pattern, which is in

TABLE VII—PHOSPHOLIPIDS OF DIFFERENT ARTERIES. CHANGES IN MEAN PERCENTAGES OF INDIVIDUAL ACIDS AND COMBINATIONS OF ACIDS WITH ATHEROSCLEROSIS

—	Aorta		Coronary arteries		Circle of Willis	
	Stage O/I	Stage II/III	Stage O/I	Stage II/III	Stage O/I	Stage II/III
Number of samples	9	10	3	4	4	4
Palmitic (16:0)	26·5	29·8	24·6	33·1	24·3	33·2
Palmitoleic (16:1)	1·1	1·0	2·7	1·4	1·9	1·7
Stearic (18:0)	19·3	15·0	14·4	14·8	17·6	13·5
Oleic (18:1)	13·1	9·8	20·8	12·4	15·7	12·1
Linoleic (18:2)	4·7	4·1	5·5	4·4	3·2	4·4
Eicosatrienoic (20:3)	1·9	1·8	1·7	1·4	1·6	0·8
Arachidonic (20:4)	10·0	8·4	9·4	6·6	7·3	4·4
Behenic (22:0)	2·5	4·5	1·8	2·3	2·8	3·5
Docosenoic (22:1)	1·0	1·0	0·5	3·4	1·9	1·2
Lignoceric (24:0)	3·6	6·3	1·8	3·0	7·2	7·1
Tetracosenoic (24:1)	1·4	4·0	1·2	5·2	3·5	6·0
Saturated	57·3	61·6	48·5	58·0	56·3	62·2
Monounsaturated	17·5	16·6	27·5	23·5	24·3	22·5
Polyunsaturated	25·2	21·8	24·0	18·5	19·4	15·3

general similar to the corresponding aortic fraction, although there are a few significant differences.

The *cholesterol ester* fatty acids (C.E.F.A.) of the coronary arteries change with increasing degree of atherosclerosis in the same way as do those of aorta, but the increase of polyunsaturated fatty acids is even greater, especially the rise in linoleic acid. The figures given for stage O/I are the mean of three analyses, two of them from coronary arteries with a mean age of $6^1/_2$ years, and the third with mean age $21^1/_2$ years. There was a considerable difference between the C.E.F.A. of these preparations at apparently the same stage of atherosclerosis. The younger arteries gave a mean percentage of 13·0 for linoleic, 17·0 for polyunsaturated acids; so it seems that there is a

* Multigraphed copies of these tables may be had from THE LANCET Office, 7, Adam Street, London, W.C.2.

relationship between the composition of the C.E.F.A. and age of the subject.

The results shown are not in agreement with those of Lewis (1958), who found a total of 81% saturated and oleic acids in the C.E.F.A. of atheromatous coronary arteries.

The rise in cholesterol-ester, linoleic, and total polyunsaturated fatty acids of the brain arteries is less than in the aorta and coronary arteries. Monounsaturated acids increase owing to an increase in oleic acid, whereas in aorta and coronary arteries there is hardly any change.

The changes in *glyceride* fatty acids of the circle of Willis are the same as in the aorta—a fall in saturated acids balancing a rise in polyunsaturated fatty acids. The coronary arteries, on the other hand, show little change in their glyceride saturated acids, the increase in polyunsaturated acids being compensated by a small (not significant) decrease in monounsaturated acids. The high content of oleic acid, both in stage 0/I and in stage II/III coronary arteries, is worthy of note. The composition of glycerides from the above-mentioned older example of stage 0/I was not noticeably different from the others.

The *free fatty acid* composition of coronary arteries and of the circle of Willis is slightly different from that in aortas, particular features being the higher content of linoleic acid and lower content of arachidonic acid in the smaller arteries. The changes with stage of atherosclerosis are also different: in the coronary arteries saturated acids (in particular palmitic acid) increase, and monounsaturated acids decrease. In the circle of Willis exactly the reverse takes place. This is in contrast to the changes in free fatty acids of aorta, which parallel those in the C.E.F.A. and glycerides, though at a low level of significance.

In the *phospholipid* fraction the summations of the fatty acids change in the same way in all three types of artery: the already high percentage of saturated fatty acids in stage 0/I increases still further with atherosclerosis; there is no change or a slight decrease of monounsaturated and a decrease in polyunsaturated acids. These changes, coupled with the observed variation of individual acids, can be attributed to an increase in the sphingomyelin content of the phospholipids (Böttcher et al. 1960). Sphingomyelin fatty acids are characterised by a high percentage of palmitic acid, a relatively small percentage of oleic acid, and the presence of considerable quantities of acids with more than 20 carbon atoms—mainly behenic, docosenoic, lignoceric, and tetracosenoic acids (Böttcher and van Gent, in the press). The initially low percentages of these higher acids, and high percentage of oleic acid, in coronary arteries indicate that the undiseased or hardly diseased coronary arteries possess a low content of sphingomyelins.

Discussion

Lipid Composition of the Three Types of Artery

The most striking feature of the lipid compositions examined is the high triglyceride content of the coronary-artery lipids. It is tempting to speculate that triglycerides may be of importance in coronary-artery metabolism and disease, especially as Schrade et al. (1959) have observed a high plasma-triglyceride level in patients with a history of coronary disease.

Almost all the changes in the lipid compositions show the same trend in the three types of artery with increasing atherosclerosis. In this sense the present results do not change the general picture of the disease built up from studies of the aorta.

Fatty-acid Compositions

The rise in the average percentage of linoleic and all polyunsaturated cholesterol esters from coronary and brain arteries is not in accordance with the hypothesis which states that the formation of atheromatous deposits is due to the deposition of relatively unsaturated cholesterol esters.

Cholesterol esters could be deposited from the plasma in a non-specific way, but this seems less probable than it did in the case of the aorta (Böttcher et al. 1960) since the percentage of dienoic acids does not reach the same value as that in the plasma C.E.F.A. of atherosclerotic patients (Schrade et al. 1959), especially as far as the circle of Willis is concerned. One may conceivably speak of a barrier—a lower permeability—to polyunsaturated cholesterol esters for the brain arteries. On the other hand, the diseased circle of Willis from a diabetic patient showed a high percentage (28·4%) of linoleic acid, though this was still not as high as in stage II and III aortas. Most of the indications are, therefore, that higher degrees of atherosclerosis are associated with higher percentages of cholesterol linoleate.

The other correlation resembling that found in aorta is the increased sphingomyelin content of the phospholipids in the more severely affected arterial wall.

Changes in the glyceride and free fatty-acid compositions are too variable to admit of interpretation at present.

Summary

The analysis of lipids extracted from intima/media preparations of relatively undiseased and of atherosclerotic coronary and brain arteries (circle of Willis) is described. The lipids were separated into phospholipids, free fatty acids, cholesterol esters, and glycerides plus free sterols. The fatty acids obtained from these four fractions were analysed by gas chromatography.

The rise in lipid content of these tissues with increasing degree of atherosclerosis is not nearly so great as in the aortas, perhaps because of the initially higher values in coronary and brain arteries.

The most striking difference between the compositions of these lipids and those from aortas (Böttcher et al. 1960) is the high percentage of triglycerides in the coronary-artery lipids (table III). The decrease in percentage of free fatty acids with increasing severity of the disease, noted previously for aorta lipids, is much less marked in the smaller arteries. Changes in lipid composition show in general the same trends in all three arteries.

In the cholesterol-ester fatty acids, an increase in the percentage of linoleic acid (and polyunsaturated acids in general) with increasing severity of atherosclerosis was observed, as in aorta lipids, although the increase is less marked in the circle of Willis.

Changes in the composition of phospholipid fatty acids indicate an increasing content of sphingomyelins in the phospholipids in atherosclerosis, as in the aorta. Glycerides and free fatty acids show characteristic differences from those of the corresponding fractions of aortic lipids (for example, a higher oleic-acid percentage in coronary-artery glycerides and a lower arachidonic-acid content in the free fatty acids of both smaller arteries), which may be of biochemical significance.

To reveal gross trends, the aorta may often be taken as a reasonable model for studies of atherosclerosis, but entire reliance on the information yielded may obscure important differences in detail existing in the smaller

arteries—differences of which the significance has yet to be elucidated.

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MEASUREMENT OF RESPIRATORY EFFORT AND ASSESSMENT OF A METHOD OF TREATING LOWER-RESPIRATORY-TRACT INFECTIONS IN SMALL CHILDREN

W. W. HOLLAND *
M.B., B.Sc. Lond.
RESEARCH FELLOW IN MEDICINE
J. R. T. COLLEY
M.B., B.Sc. Lond.
JUNIOR RESEARCH REGISTRAR IN MEDICINE
ST. THOMAS'S HOSPITAL MEDICAL SCHOOL, LONDON, S.E.1
M. A. BARRACLOUGH
M.B. Lond., M.R.C.P.
LATE HOUSE-PHYSICIAN TO THE CHILDREN'S DEPARTMENT, ST. THOMAS'S HOSPITAL, LONDON, S.E.1

Lower-respiratory-tract infections in children, which are a common cause of admission to hospital (e.g., Holland et al. 1960), comprise two main syndromes—pneumonia and bronchiolitis. In bronchiolitis the respiratory airway is usually considerably obstructed, as shown by intercostal and suprasternal recession, and, at times, wheezing. With the pneumonias, airway obstruction plays a less important part in the clinical picture. The specific treatment of these lower-respiratory-tract infections is well described in the textbooks, but no measurements of the effects of bronchodilators have been reported. This study was designed to investigate the bronchodilator effects of adrenaline in such infections.

Method

Eleven children, aged 1 month to 4 years, with lower-respiratory-tract infections, were investigated.

The method described by Dornhorst and Leathart (1952) for assessing the mechanical properties of lungs and air-passages was adapted for use in children. Intraœsophageal pressures were recorded by means of a water-filled polyethylene tube, of about 1 mm. external diameter, attached to a Hansen capacitance manometer. The free end was passed through the nose into the mid-œsophageal region. Trunk expansion was measured by a mercury-in-rubber strain-gauge plethysmograph, one limb of which was wrapped around the child's chest, and the other around the upper half of the abdomen.

* Present address: Medical Research Council Statistical Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

TABLE I—ŒSOPHAGEAL PRESSURES AND "EFFORT" OF CHILDREN WITH LOWER-RESPIRATORY-TRACT INFECTIONS BEFORE AND AFTER TREATMENT WITH ADRENALINE

Patient no.	Age	Diagnosis	Mean intraœsophageal-pressure change (cm. water)		Respiratory "effort"	
			Before treatment	After treatment	Before treatment	After treatment
1 (a)	5 mos.	Bronchiolitis	28	15	2521	1645
(b)			16	5	1494	391
2	9 mos.	Bronchiolitis	16	10	1491	1107
3	1 mo.	Pneumonia	9	10	509	576
4	2 mos.	Pneumonia	12	10	378	476
5	3 mos.	Pneumonia	10	7	651	608
6	3 mos.	Pneumonia	15	14	1716	1587
7	6 mos.	Pneumonia	12	12	549	648
8	7 mos.	Pneumonia	17	13	1261	848
9	2 yr.	Pneumonia	22	16	1538	966
10	4 yr.	Pneumonia	27	11	1421	750
11	4 yr.	Pneumonia	35	23	1668	960

All measurements were made on each child within 3 hours of admission, and again on recovery. Adrenaline was given by deep subcutaneous injection, 0·03 ml. of 1/1000 solution per lb. body-weight.

The respiratory rate and intraœsophageal pressure was measured over 20-second periods of regular respiration. The respiratory "effort" was calculated by multiplying the respiratory rate by the intraœsophageal-pressure swing on inspiration (McIlroy et al. 1954).

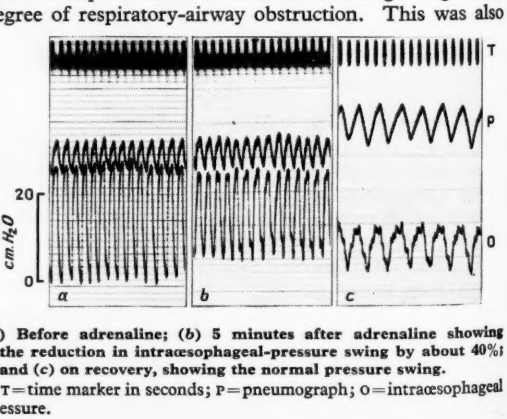
TABLE II—RELATION BETWEEN RESPONSE TO ADRENALINE, DIAGNOSIS, AND SIGNS OF RESPIRATORY-AIRWAY OBSTRUCTION

Patient no.	Respiratory "effort" after treatment (%)	Diagnosis	Signs of respiratory-airway obstruction
1 (a)	65	Bronchiolitis	Marked
1 (b)	26		
2	74		
8	67		
9	63		
10	53		
11	58		
6	92	Pneumonia	Slight
5	93		
4	126		Absent
3	113		
7	118		

Results

The results are summarised in table I. In seven of the twelve tests there was considerable decrease in respiratory "effort" after adrenaline. The average reduction is highly significant ($0{\cdot}001 < P < 0{\cdot}01$).

If these responses to adrenaline are correlated with the signs of respiratory-airway obstruction (table II), the greatest response is in the children showing the greatest degree of respiratory-airway obstruction. This was also



(*a*) Before adrenaline; (*b*) 5 minutes after adrenaline showing the reduction in intraœsophageal-pressure swing by about 40%; and (*c*) on recovery, showing the normal pressure swing.

T=time marker in seconds; P=pneumograph; O=intraœsophageal pressure.

demonstrated by the clinical response. The benefit was not limited to patients with bronchiolitis. The figure shows the changes in a child with pneumonia, although, as may be seen in table I, the greatest degree of airway obstruction was in the children with bronchiolitis. The improvement in condition was seen in children of all ages.

Discussion

Intraœsophageal pressure is easy to measure in children, who are quite tolerant of the tube once it has been inserted. In most of our cases, swings in the intraœsophageal pressure were greater than the normal (5–10 cm. water). All the children were measured again on recovery, when intraœsophageal pressures had returned to normal. Use of the strain gauge to record trunk expansion helped us to assess the effect of the bronchodilator substances by giving the respiratory rate and an approximate indication of tidal volume, as described by Dornhorst and Leathart (1952). We were unable to measure air flow directly as the children would not tolerate application of a mask or "box". We consider that the respiratory "effort", as expressed by the product of intraœsophageal-pressure swing and respiratory rate is a reasonable measurement of the respiratory "work", both before and after treatment.

Our results show that in bronchiolitis, and in some children with pneumonia, there is an element of bronchoconstriction that can be greatly reduced by adrenaline.

It is probably worth testing the effect of adrenaline in all children with pneumonia and evidence of airway obstruction.

In those children in whom adrenaline was effective, it was given by injection before feeds. We found that isoprenaline 1%, given via an atomiser into the oxygen tent or box for periods of 10–20 minutes in the hour, produced a response similar to adrenaline.

Summary

Intraœsophageal pressures and trunk expansion were measured in eleven children with lower-respiratory-tract infections before and after injection of adrenaline. The product of intraœsophageal-pressure swing and respiratory rate was taken as a measure of respiratory "effort". Those children with airway obstruction showed considerable reduction in respiratory "effort" after adrenaline.

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"... If we have managed to rationalise the way we pay for our medical service, turning it from a jumble of sudden, catastrophic expenses and haphazard charity into a regular number of shillings per week, is it ludicrously unreasonable to think we could do the same with our legal system? And while the analogy is to hand, if a complex hospital operation can be set up when necessary in a matter of hours, is it so youthfully impetuous to suggest that legal cases ought to get to court before the passage of years and the advance of old age have wiped the witnesses' memories completely blank?"—MICHAEL KAYN. *Guardian*, Nov. 3, 1960, p. 9.

IS RADIOLOGICAL EXAMINATION OF THE TWISTED ANKLE NECESSARY?

J. S. GARFIELD
M.B. Cantab., M.R.C.P.
HOUSE-SURGEON
From the Casualty Department, St. Mary's Hospital, London, W.2

THIS study was undertaken to assess the value of radiology in determining the treatment of injuries of the ankle, and to define the indications for such examination. 111 patients with twisting injuries of one ankle were seen by me in the casualty department of St. Mary's Hospital within twenty-four hours of injury. Radiographs of the ankle in the neutral position were taken in anteroposterior and lateral projections. Note was taken of the following factors:

1. Age, sex, and build.
2. Circumstances of the injury:
   a. Walking injuries, which included all twisting injuries sustained while walking on level ground, without obvious cause, due to irregularities of surface, unstable high heels, or kerbs and grass verges.
   b. Running injuries.
   c. Falling down stairs or steps.
3. The type of movement of the foot and ankle at the time of injury:
   a. A combination of inversion, plantarflexion, and medial rotation at the ankle, subtalar, and midtarsal joints was termed an *inversion injury*.
   b. A combination of eversion and lateral rotation was termed an *eversion injury*.
4. Disability after the injury was assessed simply by whether the patient could walk.
5. Pain, tenderness, bruising, and swelling were described in terms of severity and site.
6. Limitation of movement.

Results

Classification

It became clear that three groups of injuries could be defined:

1. *Major fractures.*—Radiographs showed bony damage requiring immobilisation in plaster to prevent displacement, or bony damage with displacement requiring open or closed manipulation and immobilisation in plaster.

2. *Minor fractures.*—Radiographs showed injuries such as fractures of the base of the fifth metatarsal or avulsion of cortical flakes from the malleoli, talus, navicular, or cuboid. The results of treating such injuries by strapping only were in no case worse than those treated by immobilisation in plaster.

3. *Ligamentous injury without bony damage.*—It has been said that for satisfactory diagnosis of these injuries anteroposterior radiographs must be taken with the foot held in forced inversion or eversion after injection of a local analgesic into the painful area. The demonstration of tilting of the talus has been held to be an indication for immobilisation in plaster. But in a busy casualty department it was impossible to take such radiographs as a routine measure. Moreover, in the few cases which were so examined there was greater tilt of the talus on the healthy side than on the injured side. It was decided, therefore, to dispense with such examinations, and to treat all cases in this group simply by strapping.

Analysis

The next step was to determine whether a study of the clinical features as described could indicate which patients were likely to have major fractures, which were likely to have minor fractures, and which were unlikely to have bony injury. In the first group radiological examination would be a necessary preliminary for treatment; in the

second and third groups it would be of medicolegal interest only.

Age

The patients, aged 11–60, seemed equally liable to have major fractures due to comparable types of injury.

Build

The incidence of major fractures in relation to build in patients who had " stair injuries " was:

Build	*No. of cases*	*No. of major fractures*
Fat	10	4
Normal	24	0
Thin	13	1

Circumstances of Injury

The number of major fractures associated with each type of injury was:

Circumstances	*No. of patients*	*No. of major fractures*
Walking injuries	37	2
Running injuries	13	0
Stair injuries	47	5
Miscellaneous	14	1

Of 25 patients of normal build who sustained " walking injuries " 2 had major fractures. Thus, although fat people are more liable to major fracture, such fractures cannot be excluded by consideration of build and circumstances of injury alone.

The " miscellaneous " injury which resulted in a major fracture was that sustained by a skater of normal build, aged 23, the point of whose skate was firmly fixed in the ice as he fell with eversion of the foot. (Fixation of the foot to the ground at the moment of injury demands radiological examination.) There is no doubt that any injury more severe than a " walking " one is liable to major fracture, and, irrespective of other factors, patients in these groups should all be examined radiologically.

Type of Movement Causing Injury

As all but 9 patients in this series had inversion injuries, no conclusion was reached about the relative likelihood of major fracture following inversion as opposed to eversion injury.

Disability

10 patients were unable to walk after injury; only 2 of these had major fractures. The other 6 patients with major fractures were able to walk. Thus disability is no guide to the likelihood of major fracture.

Pain

The severity of pain did not correlate with the presence of major fracture. Only near the base of the fifth metatarsal did the severity and site of the pain suggest a specific minor fracture.

Tenderness

Only in the absence of tenderness can it be said with certainty that a fracture is not present; in this series those patients with the most tenderness over bony parts and soft tissues had no major fracture.

Tenderness over soft tissues rather than over bony points does not exclude a major fracture, and probably the absence of bony tenderness has been wrongly relied upon in the past to exclude a major fracture. Only in the case of fracture of the base of the fifth metatarsal was the localisation of maximal tenderness any sure guide to the site of fracture.

Bruising

The absence of bruising did not exclude a major fracture, nor was bruising more severe in those patients with major fractures.

Swelling

All major fractures were associated with swelling, and it is probably safe to say that in the absence of swelling a major fracture is not present. Certainly the degree of swelling is related more to the severity of soft-tissue damage than to serious bony damage, and the cases with most swelling were not those with major fractures.

Limitation of Movement

In none of the patients with a major fracture did the limitation of movement differ from those with purely soft-tissue injury.

Discussion and Conclusions

Having considered the individual factors in twisting injuries of the ankle, can we define a group of clinical features which will indicate that a major fracture is not present?

Physical signs alone appear valueless, except for those patients with no swelling at all, and it is unlikely that they will reach a doctor.

The least severe circumstances of injury in this series were those of the " walking " type. There were 33 patients with this type of injury, in the 0–60 age-groups, of whom 2 had sustained major fractures:

The first was a man of 53, of normal build, who had suffered acute inversion of the right foot while walking in the street, and who had walked to hospital where he was found to have moderate tenderness in front of the lateral malleolus, and much swelling and bruising over the lateral malleolus and dorsum. Radiographs showed a horizontal fracture through the upper part of the lateral malleolus, with lateral and backward displacement of the lower fragment.

The second was a man of 26, of normal build, who had had an inversion injury while walking along a station platform. He had walked to hospital where he was found to have much tenderness and moderate bruising over and above the lateral malleolus, gross swelling of all aspects of the ankle, and moderate swelling over the lower third of the leg. Radiographs showed a spiral fracture of the lower third of the fibula.

Excluding the 2 patients with fractures of the base of the fifth metatarsal, there were therefore 31 patients, below the age of 61, who sustained " walking " injuries. Analysis of the abnormal physical signs in this group shows:

Bruising	*Tenderness*	*Swelling*	*No. of patients*	*No. of major fractures*
+	+	+	6	2
−	+	+	11	0
−	+	−	11	0
−	−	+	2	0
+	−	+	1	0

Thus only 6 patients had a combination of moderate (or severe) tenderness, swelling, and bruising, these including the 2 cases of major fracture. All the other patients in this group lacked one or more of these abnormal physical signs.

Therefore clinical features alone give an unequivocal guide to diagnosis in three groups of cases:

The absence of any swelling is a firm indication of the absence of any significant bony or ligamentous damage whatever the circumstances of injury.

Tenderness localised to the base of the fifth metatarsal is a sure indication of fracture in this site only.

The absence of moderate tenderness, bruising, or swelling in a patient under 61 who injures the ankle while walking is a good indication that there is no major bony injury.

In this series of 111 cases there were 41 patients in these groups. I would suggest that patients in any of these three groups do not require radiological examination for the determination of treatment; such cases may well be treated by the general practitioner without reference to hospital.

Summary

111 cases of injury to the ankle were studied clinically and radiologically.

It is possible clinically to define three groups in which radiological examination is unnecessary for determining treatment.

In the remaining cases clinical features give only an inaccurate guide to the nature of the injury, and in these radiological examination is necessary.

It seems that the whole question of the diagnosis of ligamentous injuries of the ankle requires re-examination.

I should like to thank Mr. G. L. W. Bonney for much help and advice in the preparation of this paper.

VOLUME REGULATION AND RENAL FUNCTION IN ANALBUMINÆMIA

H. BENNHOLD
M.D.
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF TÜBINGEN AND DIRECTOR OF THE MEDICAL CLINIC

D. KLAUS
M.D.

P. G. SCHEURLEN
M.D.

MEDIZINISCHE UNIVERSITÄTS-KLINIK UND POLIKLINIK, TÜBINGEN

DURING the past few years, we have had under observation a brother and sister who, because of a recessive gene, have a complete lack of serum-albumin (Bennhold et al. 1954, Bennhold 1956, Bennhold et al. 1958, Bennhold and Kallee 1959). These two cases of analbuminæmia show no disturbance of water and electrolyte balance, and are clinically healthy, though the plasma osmotic pressure is reduced from the normal of 25–30 mm. Hg to 10–14 mm. Hg.

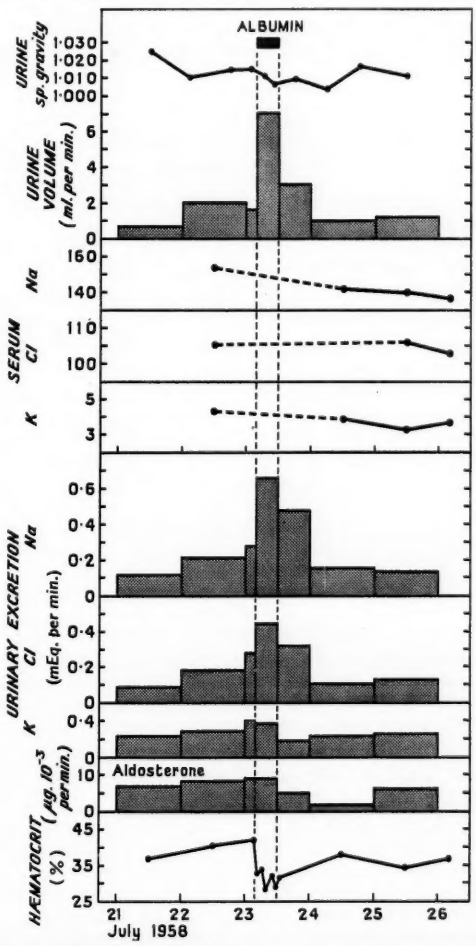
Our examinations showed that this low osmotic pressure is compensated by a marked drop in the capillary hydrostatic pressure, so that capillary tests showed some noteworthy findings. The hydrostatic pressure in the glomerular capillaries is lowered, with the result that glomerular filtration is at the lower limit of normal (see table). Normal glomerular filtration is maintained, because the renal blood-flow is already reduced in the preglomerular vessels, as shown by the reduction in renal plasma-flow. 2 days after the infusion of 150 g. of human albumin in 3000 ml. isotonic glucose-saline solution, the plasma osmotic pressure rose to an average of 20 mm. Hg; at the same time the renal blood-flow increased. Since the cardiac minute-volume, measured by the method of Broemser and Ranke, showed no change at that time (3600–3200 ml.), it may be assumed that the adaptation of the renal blood-flow to the lowered osmotic pressure is mainly brought about by vasoconstriction of the afferent arterioles.

Balance studies were made on two occasions, a year apart. During each study, an intravenous infusion of 150 g. of human albumin in 3000 ml. of isotonic glucose-saline solution was given over a period of 8–9 hours. These studies showed that in analbuminæmia the isotonic expansion of the extracellular space is balanced by a rapid diuresis (see figure). In a healthy person given isotonic or hypertonic albumin solution only a water diuresis results (Strauss et al. 1951, Smith 1957), but in the analbuminæmic patient there is an additional Na^+ and Cl^- diuresis, so that the water and sodium chloride given is excreted within 24 hours. In analbuminæmia,

RENAL HÆMODYNAMICS, AND WATER AND ELECTROLYTE EXCRETION IN ANALBUMINÆMIA. TESTS UNDER CLEARANCE-CONDITIONS, 1 DAY BEFORE AND 2 DAYS AFTER INFUSION OF 150 G. HUMAN ALBUMIN. CORRECTED TO 1·73 SQ. M. BODY-SURFACE

—	Day 1	Day 2	Δ (%)
Urinary concentration (mEq. per litre):			
Sodium	152·5	152·0	..
Chloride	124·1	132·1	..
Potassium	13·0	13·9	..
Urinary output (μEq. per minute):			
Sodium	722·0	466·0	..
Chloride	589·0	404·0	..
Potassium	61·8	42·5	..
Urinary clearance (ml. per minute):			
Sodium	4·58	3·09	−32·5
Chloride	4·94	3·58	−27·5
Potassium	13·75	12·30	−10·5
Water	4·74	3·05	−35·6
Extraction fraction (%):			
Sodium	4·89	4·01	−18·1
Chloride	5·26	4·64	−11·6
Potassium	14·7	16·0	+ 8·9
Tubular reabsorption:			
Sodium	95·1	96·0	+ 0·8
Chloride	94·3	95·7	+ 1·5
Potassium	84·8	83·6	− 0·9
Water	95·1	96·3	+ 1·1
Inulin clearance (ml. per minute)	93·7	77·1	+17·7
p-amino-hippuric acid clearance (ml. per minute)	243·0	334·0	+37·1
Filtration fraction (%)	38·6	23·2	−40·0
Serum-albumin (g. per 100 ml.)	0·03	2·34	..

Δ% = difference, expressed as a percentage, between values on day 2 and day 1.



Urine-volume, electrolytes in serum and urine, aldosterone-elimination, and hæmatocrit values before, during, and after albumin infusion on July 23 (150 g. human albumin in 3000 ml. isotonic saline-glucose solution, given from 12 noon to 8.15 p.m.).

aldosterone excretion is normal; it decreases after the albumin infusion. There is a definite time-lag, however, between maximum sodium diuresis and a fall in aldosterone excretion (see figure). Clearance studies showed that during the albumin-lack the tubular reabsorption of extracellular electrolyte and of water is diminished. In analbuminæmia, therefore, even small quantities of isotonic saline (200–300 ml.) cause a considerable sodium-chloride diuresis. To achieve equally high excretion fractions in a normal person, saline infusions either 8–10 times greater in volume or 3 times more concentrated would be needed (Strauss et al. 1951, Smith 1957, Ladd 1951a, 1951b).

The lowering of the capillary hydrostatic pressure and the rapid sodium-chloride diuresis resulting from small volume changes explains why, as is described in detail elsewhere (Scheurlen and Klaus 1960), in analbuminæmia, no disturbance of the water and electrolyte balance takes place, in spite of the very low osmotic pressure.

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COLD INJURY
AMONG CHILDREN SEVERELY ILL IN THE TROPICS

D. C. MORLEY
M.A., M.D. Cantab., D.C.H.
ASSOCIATE LECTURER IN PÆDIATRICS, UNIVERSITY COLLEGE, IBADAN
From the Wesley Guild Hospital, Ilesha, Nigeria

COLD injury in small infants, as described by Mann (1955), Mann and Elliott (1957), and Bower et al. (1960), is now well recognised by doctors looking after small children in temperate climates. Nassau (1948) also showed that cold injury can arise in subtropical areas, such as Palestine. In the Wesley Guild Hospital, kwashiorkor accounts for a sixth of all the children admitted. A fairly common syndrome in such children is a slow pulse-rate and more than the usual lethargy. This had been noted for more than a year before it was discovered to be sometimes associated with a subnormal temperature. In this paper I shall describe the condition of low temperature, or cold injury, in older children.

The Study

During July–September, 1958, I took the temperature of all children who felt cold, using a low-reading clinical thermometer. Any child found to have a temperature below 95°F (35°C) was considered to have cold injury. During the three months 18 such children were seen among the 315 admitted to the children's ward; in addition 1 child was seen in a village hut. Table I gives some details of these children.

All these children felt cold to the hand, but they could be distinguished from children with peripheral circulatory failure because the axilla also felt cold.

The most unusual feature of this series is the number of older children that it includes. The following case-histories are examples of subnormal temperatures in such older children:

Case 1.—A Yoruba girl of 8 years was seen in a village in which the hospital is undertaking a longitudinal study of a group of children. The mother was mentally unstable; her husband had left her, and the family would not assist her. The child had first been seen in 1957 with œdema, puffiness of the face, and the skin changes of kwashiorkor; her mother had been supplied with protein supplements, and the child's condition had temporarily improved. The protein foods were given intermittently over the next year without much cooperation from the mother; the child's condition deteriorated, and she started to have diarrhœa towards the end of July, 1958, As she was not brought to the dispensary, I visited her house in the village. She was found lying semi-conscious by the embers of a fire, with only one small piece of cloth over her. She was taken to the dispensary where rectal temperature was found to be only 93·4°F (34·1°C); an attempt was made to warm her up but she died eight hours later.

TABLE I—SUBNORMAL TEMPERATURES IN 19 NIGERIAN CHILDREN (JULY–SEPTEMBER, 1958)

Diagnosis and no. of cases	Ages of children	Lowest recorded rectal temperature (°F)	Outcome—Living or dead
Kwashiorkor (8)	8 yr., 7 yr., 6 yr., 3 yr., 2¾ yr., 2 yr., 1 yr., 1 yr.	93·4, 92·0, 93·4, 94·4, 92·6, 94·6, 94·8, 94·4 (*33·3–35·8°C*)	5 living 3 dead
Acute diarrhœa (5)	2 yr., 1½ yr., 1 mo., 1 mo., 1 mo.	94·2, 93·8, 94·2, 94·6, 93·2 (*34–34·8°C*)	1 living 4 dead
Acute osteomyelitis (2)	3 mo.; 11 days	93·6, 93·4 (*34·1–34·2°C*)	1 living 1 dead
Sickle-cell anæmia (1)	7 yr.	91·4 (*33°C*)	1 living
Other conditions (3)	35 days, 17 days, 11 days	94·6, 94·8, 92·4 (*33·6–34·8°C*)	2 dead 1 living

This was the only child in this group who was seen with hypothermia in her home and not in hospital, but this is not surprising as doctors in this country rarely get an opportunity of seeing children in their homes.

Case 2.—A boy aged 2 years, with the typical appearance of kwashiorkor, was brought from a village 30 miles from Ilesha by his parents. He had œdema, and small areas of skin changes of the " enamel paint " type. 3 days after admission to hospital his temperature dropped to 94·6°F (34·8°C). He was warmed up, but his temperature was unstable for a further five days. He was sufficiently improved to be discharged home after fifteen days. He was seen only once as an outpatient, and at that time he was recovering well.

Case 3.—A 7-year-old boy was admitted comatose and apparently moribund. His parents gave a history of eight hours' coma, and they had noticed he had become cold in the night. His hæmoglobin was 18% (2·7 g. per 100 ml.) He was given an immediate blood-transfusion, and soon recovered consciousness. He was apparently well within twelve hours, and was discharged on the third day. Examination of his blood had shown a high proportion of sickled cells.

The main feature of interest in this group is the number of children, over a year old, with subnormal temperatures. In many of these children the ability to maintain body temperature seemed to be lost for several days. Their temperatures repeatedly fell unless they were well covered with blankets, and for several an electric blanket was used as a temporary external source of heat.

The child in temperate climates depends for warmth on a heated house and an adequate supply of clothing.

TABLE II—MONTHLY MEAN MAXIMUM AND MINIMUM TEMPERATURES (°F) FOR 1958, AT OSHOGBO, 25 MILES FROM ILESHA

—	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Maximum ..	92	94	93	89	88	86	84	82	83	85	87	90
Minimum ..	70	68	74	73	71	71	68	68	70	70	71	71

The children in this community live in houses where any form of heating is unusual, the temperature usually being similar to that outside (table II). The clothes worn by small children are usually cotton, although a few babies wear wool. The small child and the sick child depend on the warmth of the mother's body. Throughout the day the child is carried on her back, and at night he sleeps very close to the mother, usually with the nipple in his mouth if still breast feeding. If a child is sick and the mother has a younger child on her back, she arranges for someone else to carry the baby and carries the sick child herself. Friends and relatives, except her own mother, are unwilling to carry a sick child. The mother appreciates the importance of warmth to a sick child, and nurses in hospital may have difficulty in persuading mothers not to put small children on their backs. In many hospitals the mothers are sent away at night, but there are still a few hospitals which make it possible for the mother and child to sleep close together.

The Yoruba child or adult takes his bath regularly, and mothers usually bath their children in the morning. Water is seldom heated, and when the bath is over the mother will put the child on her back to become warm again. In hospital, too, the child may be bathed in unheated water, but the mother will not be there, or if she is she may not be allowed to place her child on her back. Really adequate bed coverings are exceptional, and a poor substitute for the mother's body heat.

Table I suggests that subnormal temperature is most common in children with kwashiorkor, the acute manifestation of the protein shortage that is almost universal among the children attending hospital in this area. Lethargy is one of the most striking features of all stages of this condition, and there is also much muscular wasting. The child with kwashiorkor seems to be incapable of shivering, and none of these cold children were seen to shiver. The other feature common to most of these children was prolonged diarrhœa with variable loss of fluid and electrolytes.

Discussion

The condition of subnormal temperature was commented on by Kahn (1959), who considered a temperature below 95°F to be a grave prognostic sign in children with kwashiorkor. Of 100 such cases which he described, 5 had low temperatures, and of these only 1 recovered. Kahn suggests this condition may be associated with a low serum-potassium level; such estimations were not possible in this hospital when these cases were seen.

Experiments on several species of animals (Adolph 1951) suggest that the newborn animal can survive a low temperature which would be fatal a few weeks later. In the rat the transition to the adult intolerance of hypothermia occurs at about the age of 3 weeks. The older child similarly appears less able to withstand the effects of a low body temperature.

In the cases described here it was sometimes difficult to warm the child. Hot-water bottles are not effective, and an electric blanket could apparently be dangerous because the child might be warmed too quickly and then collapse. Re-warming by close contact with the mother seems to have much to recommend it.

In the twenty months since these cases were studied an effort has been made to prevent this condition in the ward. Mothers are encouraged to keep in close contact with their sick children, and blankets are more widely used. The nurses are alive to the condition and report any child whose temperature falls below 97°F (36·1°C), low-reading clinical thermometers then being used on such children. Another 37 children have been seen with temperatures below 95°F, of whom 15 were over a year old, and of these 9 have died.

Summary

In a hospital in Nigeria 19 children were seen within three months with temperatures below 95°F. 9 of these children died. The commonest clinical diagnosis was kwashiorkor, this being found in 8 of the 19 children.

Separation from close contact with the mother is suggested as the principal reason for this condition arising in these sick children.

I wish to thank members of the children's department of King's College in the University of Durham, Newcastle upon Tyne, for their help in preparing this paper. The Nigerian Meteorological Service supplied the data on temperature at Oshogbo. This work has been assisted by the West African Council for Medical Research.

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EOSINOPHILIC PHLEGMON OF THE ALIMENTARY CANAL CAUSED BY A WORM

F. C. KUIPERS
M.D. Leiden
PATHOLOGIST, MUNICIPAL HOSPITALS, ROTTERDAM

P. H. VAN THIEL
Ph.D. Leiden
PROFESSOR OF PARASITOLOGY, LEIDEN

W. RODENBURG
SURGEON, MUNICIPAL HOSPITAL, BERGWEG, ROTTERDAM

W. J. WIELINGA
M.D. Groningen
SURGEON, MUNICIPAL HOSPITAL, COOLSINGEL, ROTTERDAM

R. TH. ROSKAM
DIRECTOR CHEMICAL DEPARTMENT,
STATE INSTITUTE FOR FISH INVESTIGATION, IJMUIDEN

THIRTEEN patients with a more or less localised eosinophilic phlegmon in the alimentary canal were seen in 1955–59. This lesion, which does not seem to have been described previously, appeared to be caused by a parasite, identified as the larva of *Eustoma rotundatum*. Most of the patients were infected by eating slightly salted raw herring.

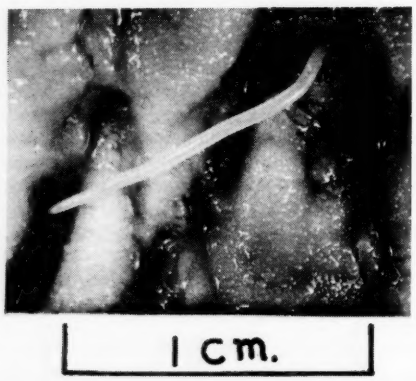
This paper describes the disease and also an investigation into the occurrence of *E. rotundatum* in North Sea herring.

Illustrative Case-report

On July 26, 1955, a man aged 51 was admitted to the surgical department of the Bergweg hospital in Rotterdam. For a few hours he had had attacks of colicky pain in the lower abdomen, rapidly increasing in severity and frequency. He had nausea, but did not vomit. There was no history of previous abdominal complaints. He had a temperature of 37·7°C (100°F); a pulse-rate of 92.

The abdomen was not distended, and moved well with respiration; there was no visible peristalsis. On coughing, pain was felt in the right lower abdomen which was also painful to percussion. Peristalsis was active. Splashing could not be elicited. No rigidity of the abdominal muscles. Tenderness of right lower abdomen. Local rebound tenderness was severe. Rectal examination was painful. The diagnosis of acute appendicitis was made—though with some reservation.

At laparotomy there was a fair amount of clear, light-yellow fluid in the abdomen; the appendix was not inflamed. The distal coils of the ileum were swollen and hyperæmic. The



Ulcer of small intestine, showing larva of *Eustoma rotundatum*.

serosa was covered with fibrin. About 30 cm. from the ileocolic valve there was a firm infiltration the size of a chestnut on the mesenteric border of the intestine. An ulcer crater could be felt within this area. The small intestine was not distended. The mesentery was obviously œdematous. The lymph-nodes were not enlarged.

The inflamed part of intestine was resected. The patient was given penicillin and streptomycin. The postoperative course was uncomplicated. Pathological examination of the resected specimen revealed an ulcer 1·5 cm. in diameter, out of which a worm 1·3 cm. long was protruding (see figure). The mucosa was œdematous. The serosa was also thickened and covered locally with fibrin.

Microscopically there was an eosinophilic phlegmonous enteritis with ulceration at the site of the worm. Cross-sections of the worm could be seen in the submucosa of serial sections of the specimen.

Other Patients

In twelve patients the lesion was confined to the small intestine. All were acutely ill shortly before admission; the most obvious sign being colicky abdominal pain. The previous history did not usually produce much relevant information. Only a few patients had had vague abdominal complaints beforehand.

On physical examination, apart from signs of irritation of the peritoneum, there were usually signs of an incomplete ileus of the distal small intestine.

On admission, the temperature varied between 36·2°C (97°F) and 37·8°C (100°F). Six patients had a leucocytosis; the eosinophils were counted twice, and in both cases normal figures were obtained. In eleven patients the signs were so alarming that laparotomy was carried out within a few hours after admission. Only one patient was treated conservatively for 14 days. When the symptoms did not disappear, an exploratory laparotomy was done. The inflamed intestine was resected in all twelve patients. In all the typical picture of eosinophilic phlegmon was found; and, without exception, the same parasite or—as in the case not operated upon immediately—the remnants of one were found in the centre of the lesion. A pre-operative diagnosis of duodenal ulcer was made in the thirteenth case.

This patient, a man aged 43, had had gastric complaints for 6 months that did not improve with conservative therapy. The X-ray photograph supported the diagnosis of duodenal ulcer. At operation, an infiltration the size of a cherry was found 8 cm. proximal to the pylorus on the greater curvature of the stomach. The duodenum was normal. Partial gastrectomy was carried out. The lesion appeared to consist of an eosinophilic phlegmon in the centre of which remnants of the parasite were found.

The postoperative course in ten patients was completely normal. Two patients died a few days after the operation from a staphylococcal enteritis. They both received oxytetracycline in the postoperative period. In one patient a leaking of the anastomosis resulted in peritonitis on the 6th postoperative day. The patient recovered after resuturing. In three patients slight eosinophilia was established at a varying length of time after the operation. In nine patients the fæces were investigated for parasites several times; the result was negative 8 times. Ascaris eggs were found in one patient.

Ten of the surviving eleven patients were free from complaints at follow-up. 8 weeks after the first operation one patient underwent a second laparotomy for ileus caused by adhesions. No trace could be found of the original process.

Ætiology

It was not until the summer of 1958 that we were able to identify the parasite with certainty after obtaining an intact worm, by macerating a section of resected intestine for several weeks. It appeared to be a larva of one of the Heterocheilidæ. These parasites belong to the family of the Ascarides, and occur in many fresh and salt water fish and in earthworms.

A detailed history especially as regards the eating of fish was taken from the seven patients known and alive at that time. The only fish that all those interrogated had eaten was so-called " nieuwe haring " (raw herring)—sometimes as many as 20 per day. The association with the consumption of herring was still more probable when we realised that all these patients became ill between May and August. These are the months in which by far the greatest number of herrings are eaten.

After the opening of the herring season in 1959, Dr. C. F. A. Bruyning was fortunate enough to be able to obtain the parasite from a recently caught herring. It turned out to be *E. rotundatum*, one of the Heterocheilidæ (van Thiel et al. 1960). It was now practically certain that the disease was associated with herring. The occurrence of this parasite and its behaviour in fresh and salted herring was investigated by the Rijksinstituut voor Visserij-onderzoek (State Institute for Fish Investigation). It soon appeared that North Sea herring were highly infected with larvæ of *E. rotundatum* and that the degree of the infection increased with the length of the herring—i.e., with its age (see table). In freshly caught herring, the larva was found in the peritoneal cavity. When some time had elapsed before the examination, some parasites were found to have migrated into the flesh.

Before consumption, the peritoneal cavity is cleaned and its contents are removed. Only the parasites in the flesh are left behind, and it is these larvæ that are likely to be the cause of the disease in man.

The methods of preservation of herring seem to play a part. In herring that are cooled on ice without further preparation, the number of larvae that migrated from the peritoneal cavity into the flesh was much higher than in herrings salted at sea

NUMBER OF EUSTOMA LARVÆ ISOLATED BY PEPSIN DIGESTION FROM HERRING CAUGHT IN THE NORTH SEA

Length of herring	Number of herrings investigated	Number of eustoma per 100 herrings	
		In the flesh	In the gut
20–24 cm. (small)	700	0·14	5·3
24–28 cm. (average)	207	9·6	57
28–32 cm.*	184	24	580

* Herrings of this size are hardly ever eaten raw.

directly after being caught. It appears that salt has a paralysing action on the larvæ. This paralysing action is directly proportional to the salt content. Nevertheless, a few larvæ were found in the flesh of normally salted herring.

Herrings preserved in a combination of vinegar and kitchen salt are regularly eaten in the Netherlands. It appeared that the maximal survival time of eustoma larvæ in this mixture was ±25 days at 0°C. The larva is almost completely resistant to gastric acid.

The chance of a person consuming a larva of eustoma is 0·14% with small herrings, 9·6% with larger herrings (see table). Thus one would expect far more cases of the disease from the millions of raw herrings eaten annually than the thirteen described in this article. It is unlikely that there have been any other cases of the disease in the Netherlands. The pathological picture is so obvious that it would be easily recognised. From the results of a questionnaire sent to the pathologists in the Netherlands in January, 1959, it appeared that none of them had ever seen such a specimen before. Hence the first infection with a eustoma larva is unlikely to give rise to the disease picture described. It is possible that the disease only develops after a second or a third worm penetrates into the intestinal wall within a period of time suitable for sensitisation to arise. The clinical and histological picture could also indicate such an allergic reaction.

It is also remarkable that of the thirteen patients described, eleven live in Rotterdam or its immediate vicinity. Rotterdam has from early times been of the most important markets for herring, and it is common practice there to eat slightly salted herring. The majority of the patients questioned ate very many raw herrings. Thus they ran a greater risk of becoming sensitised.

Finally, it seems to us that it is not impossible that this disease is observed in other countries or islands around the North Sea. Although the patients described here were almost certainly infected by raw herring, the possibility remains that the consumption of other uncooked slightly salted fish may have caused the syndrome in other cases.

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Preliminary Communication

TRANSMISSION OF SERUM PROTEINS FROM FŒTUS TO MOTHER IN THE RHESUS MONKEY

INDWELLING CANNULATION OF FŒTUS WITHOUT INTERRUPTION OF PREGNANCY

It has been shown that some serum proteins (antibodies in man,[1] ^{131}I-labelled albumin and globulin in monkeys [2 3]) are transmitted from mother to fœtus in utero in primates. Nothing is known about the transfer of proteins from the fœtal circulation to the mother's.

We report here evidence that ^{131}I-labelled albumin and γ-globulin can be transmitted, probably selectively, from fœtus to mother in the rhesus monkey, in which the placental system is closely similar to that of the human and unlike that in orders other than primates. To obtain this evidence, direct access to the fœtus was necessary so that the dose of ^{131}I-labelled serum proteins could be injected into the fœtus. We have found that this access can be obtained at open operation in utero, and that an indwelling cannula can be left in the fœtus, without the interruption of pregnancy and with the birth of normal living babies some weeks later.

METHODS

Fœtal rhesus serum (15–25 mg. protein) was labelled with ^{131}I (1·0–1·5 mC) at a level of less than one iodine atom per molecule.[4] Three rhesus monkeys, A, B, and C, weighing 4–5 kg. and estimated to be 12–16 weeks pregnant were used. Each monkey was given carrier iodide in the drinking-water one day before operation, and/or an intravenous injection of sodium iodide (10 mg.). They were anæsthetised with thiopentone sodium followed by nitrous oxide, trichlorethylene, and sometimes ether; gallamine triethiodide was used as a muscle relaxant, and progesterone (50 mg.) in oil was given intramuscularly. A midline incision was made in the upper or the lower segment, and the liquor amnii aspirated through the unopened membranes. The fœtus was exposed and the dose was injected into a placental vein in monkey A, and into the fœtal peritoneum in monkey B: great care was taken to demonstrate that no leak had occurred and that the dose had not been misplaced. The uterus was then closed and the warmed liquor reinjected into the amniotic cavity.

After the uterus had been opened in monkey C a cannula containing heparinised saline solution was inserted into the peritoneal cavity of the fœtus through a stab incision and anchored to the sutures closing the fœtal skin. The cannula was brought out through the incision in the uterus and abdominal wall, and the sealed end anchored under the skin of the mother's flank. The uterus was repaired and the liquor reinjected. 6 days later the sealed end of the cannula was exposed through a small skin incision and the dose, followed by heparin saline, injected into it. Samples of blood and liquor were taken from each monkey 1 and 4 hours after the dose and at intervals thereafter. The serum proteins were separated by electrophoresis on cellulose columns and by chromatography on D.E.A.E. cellulose as described for previous experiments.[3]

RESULTS

Monkey B aborted after 24 hours; no fœtal movements were felt in monkey A after 48 hours; monkey C gave birth to a normal baby 7 weeks after operation. In all three cases, however, the general findings in the maternal serum and liquor amnii were similar. In the maternal serum, radioactivity was first found in the albumin fraction 18 hours after injection, and increased in concentration in samples taken up to 8 days after operation. Radioactivity in the γ-globulin fraction isolated by electrophoresis and by chromatography appeared at 24 hours and also increased in concentration in the samples taken up to 8 days later. Other serum proteins were not isolated and measured individually. The general electrophoretic pattern, however, showed that little radioactivity occurred in the electrophoretic fractions between the albumin and the γ-globulin. In this respect, the maternal serum samples were quite different from (1) the dose material, (2) serum recovered from the fœtus aborted 24 hours after the dose (monkey B), and (3) serum taken from an adult and from a month-old baby up to 8 days after being given a similar dose of ^{131}I-labelled fœtal serum.

Because the dynamics of the system were so complex, no attempt was made at quantitative estimation of the percentage of the dose transferred. The amounts of protein transferred, however, were small.

Samples of liquor taken at successive intervals after injection contained increasing quantities of radioactive iodide (presumably from catabolism of proteins in the fœtus), but virtually no radioactivity in the proteins precipitated by trichloracetic acid.

DISCUSSION

We found previously [3] that ^{131}I-labelled albumin and γ-globulin are transferred, apparently selectively, from the mother to the fœtus in the monkey. The liquor

1. Brambell, F. W. R. *Biol. Rev.* 1958, **33**, 488.
2. Bangham, D. R., Hobbs, K. R., Terry, R. J. *Lancet*, 1958, ii, 351.
3. Bangham, D. R. *J. Physiol.* 1960, **150**, 250.
4. McFarlane, A. S. *Nature, Lond.* 1958, **182**, 53.

amnii did not play a significant part in this transfer. The experiments described above show that both albumin and γ-globulin can return to the mother. There is therefore a constant exchange of these two proteins between mother and fœtus. In view of the negligible quantity of labelled serum protein going from fœtus to the liquor, it seems unlikely that this is the route of return to the mother.

In so far as ^{131}I-labelled serum proteins can be assumed to behave biologically like unlabelled proteins, it appears from these experiments that the transfer of albumin and γ-globulin from the fœtus to the mother is selective (little radioactivity was found in the α-globulin and β-globulins), although other individual serum proteins were not specifically isolated and studied. We have studied several fœtal rhesus monkeys with genetic variants of β-globulin, isolated by starch gel electrophoresis, quite different from those in the mother's serum. Although some of the variant β-globulins occur in both mother and fœtus, some variants are found only in one or the other; the pattern of variants in the liquor always corresponds to that in the maternal serum. This is collateral evidence that there is little transfer of at least some variants of β-globulins from fœtus to liquor or to mother, or vice versa. In our previous experiments [2 3] we found that the albumin in the liquor exchanged rapidly with the mother's intravascular serum albumin. The additional experiments, described above, show that little of the serum proteins which occur in the liquor in mid-pregnancy can be derived from the fœtus.

Our experience with the first two monkeys corresponds with that of other workers operating on rhesus monkeys.[5] We have, however, previously had some monkeys whose pregnancies survived similar operations for 2–7 weeks.

By modifying our method, we have found it possible to perform a hysterotomy and implant an indwelling cannula in a fœtus in utero without interrupting pregnancy. After the last four such operations normal living babies have been born naturally 6–7 weeks postoperatively.

SUMMARY

^{131}I-labelled homologous fœtal serum proteins were injected intravenously and intraperitoneally at open operation and intraperitoneally through a cannula into the fœtus 6 days after operation, in monkeys in mid-pregnancy.

^{131}I-labelled albumin and γ-globulin, isolated by electrophoresis and chromatography, were found in samples of maternal serum taken 2–8 days afterwards. This transmission is selective, at least for these two proteins, and presumably takes place across the fœtal placenta. Negligible amounts of radioactive protein were found in the liquor amnii.

The experiment on the third monkey, together with subsequent experience, shows that it is possible to perform open operation on the fœtus in utero in mid-term pregnant rhesus monkeys without interrupting pregnancy or prejudicing the birth of a normal baby.

It is a pleasure to thank Mr. R. C. Holloway for help in the iodination of the serum, and Miss Sheila Macdonald for her assistance.

D. R. BANGHAM
M.B. Lond.
K. R. HOBBS
D. E. H. TEE
M.B. Lond.

National Institute for Medical Research, Mill Hill, London, N.W.7

5. Ramsey, E. M., Corner, G. W., Jr., Long, W. N., Stran, H. M. *Amer. J. Obstet. Gynec.* 1959, **77**, 1016.

New Inventions

A BLOOD-TRANSFUSION BOTTLE HEATER

IN exchange transfusions the problem of uncertainty about blood temperature has never been entirely resolved by warming the blood bottle in water before transfusion. Blood flowing along the polyethylene tube has often been palpably cool, and this has not helped to reduce shock or vascular spasm. A search was therefore made for a suitable bottle heater which would warm the blood to an optimum temperature. After much work by Electrothermal Engineering, Ltd., an apparatus was designed to bring the blood to 37°C and to keep it at this temperature during transfusion. This has been proved satisfactory in two years' use.

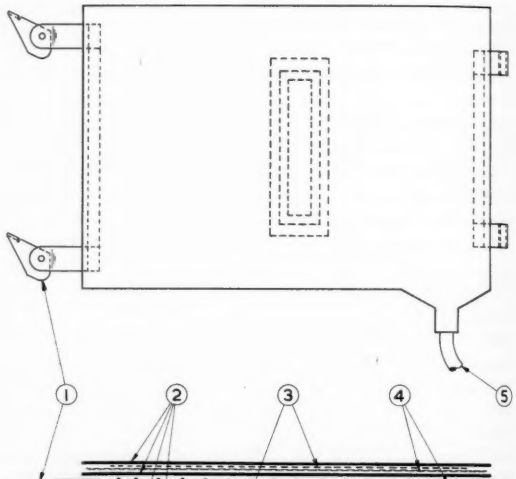

Fig. 1—Plan and diagrammatic section through heater.
1=quick-release fasteners, 2=rubber sheet, 3=wire-earthing mesh, 4=glass cloth, 5=mains supply lead, 6=element wire, 7=thermostat, and 8=thermostat housing.

The heater (fig. 1) measures 8·85×6 in. overall, and is designed to fit snugly and securely around the suspended bottle. The heated area extends within $^1/_2$ in. of each edge, and measures about $7^3/_4 \times 5^1/_4$ in. The heater is made of a nickel/chrome element spiralled on to a rayon core, and firmly sewn to a single layer of closely woven glass cloth. The heater, in this state, is then sandwiched between natural rubber sheets $^1/_{16}$ in. thick. Woven-wire earth screens are then applied to each side of the heater, and they in turn are covered by a second layer of $^1/_{16}$ in. sheeting. A rubber-housed miniature preset thermostat is built into one side of the heater, ensuring that the correct temperature is continuously maintained. Quick-release metal fasteners are fitted to both 6 in. edges, enabling the heater to be quickly and easily fitted (fig. 2).

Fig. 2—The heater in position.

The heater is equipped with 6 ft. of three-core rubber-covered lead, the main connection of which is made before the final moulding

process. The total loading of the heater is 50 watts, and it is designed for operation from a 230/250 volt mains supply. To prevent traction on, and distortion of, the electrical cable a drip stand has been adapted by incorporating an electrical plug at the base.

Thanks are due to Dr. P. A. S. Edmunds, my late registrar, who suggested the possibility of this method of heating; to Mr. H. Glynne Jones, hospital secretary, and Mr. P. Convey, group supplies officer, for enthusiastic help; to Mr. H. Leach for the photographs; and to the manufacturers, Electrothermal Engineering, Ltd., 270, Neville Road, London, E.7, for the diagram.

St. David's Hospital, Bangor GWYN GRIFFITH M.D. Lpool, F.R.C.P.E., D.P.H., D.C.H.

Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION

THE Association's annual meeting was held in Leeds and Harrogate on Oct. 27–29, under the presidency of Mr. H. J. SEDDON.

During the meeting Sir CHARLES MORRIS, vice-chancellor of the University of Leeds, described the organisation which was being set up to help the newly independent countries. The Commonwealth Education Conference met in Oxford in 1959 to discuss the supply of technologists and teachers to the underdeveloped and newly independent countries. It was obvious that for a long time supply would fall well short of demand, but there was great determination that something must be done and legislation (the Commonwealth Scholarship Act) had been passed to this effect. 500 scholarships had been made available in this country, 250 of them to be given each year. The idea was that the scholars should come here for postgraduate study after they had taken their first degree. This scheme was organised by the Government but was run by the universities, which were anxious to help. The newly developed countries had already had substantial sums of money to help them to develop their own universities up to the level of the first degree, and the U.S.A. and Canada and other countries had been helping with this. Efforts were being made to second our own university teachers to these new universities; but it was difficult to find men willing to go away, leaving families and career for three to five years. Nevertheless, the scheme generally had got off to a good start.

Mr. SEDDON asked whether it was desirable for private arrangements along these lines to be made, such as had been made in the case of Hong Kong. Sir CHARLES MORRIS replied that in such a clear-cut case the answer was Yes, and the authorities would no doubt help so long as money was available.

Sir HARRY PLATT said that this was a very heartening communication. But many committees were trying to carry out the same programme in these underdeveloped countries; and there seemed to be little coordination between them, each country acting independently. This would lead to confusion. Greater coordination would lead to economy of effort and manpower. Sir CHARLES MORRIS replied that the Vice-Chancellors' Committee was in touch with similar bodies in other countries and regular meetings were held to ensure coordination.

Mr. J. EDELSTEIN (South Africa) said that many men came to this country from South Africa to complete their education. Their own medical schools were now being formed, and the scheme mentioned was very welcome.

Mr. H. OSMOND-CLARKE (London) asked what was the mechanism whereby a man in one of the countries could apply for a scholarship. Sir CHARLES MORRIS said there was an organisation in each country for this, and he could apply to his university or the British Council. There was an inter-university unit in this country to coordinate arrangements.

Reviews of Books

Encyclopædia of Urology

Editors: C. E. ALKEN, Homburg, Saar; V. W. DIX, London; H. M. WEYRAUCH, San Francisco; E. WILDBOLZ, Berne. Berlin: Springer. 1960.

Vol. III. *Symptomatology and Examination of the Blood, Urine and Genital Secretions.* Prof. KARL HINSBERG, DR. PHIL., direktor des Physiologisch-chemischen Institutes des Medizinischen Akademie, Düsseldorf; Prof. JOSEF KIMMIG, DR. MED., DR. PHIL., direktor der Universitats-Hautklinik und Polyklinik, Hamburg; with JOHANNES MEYER-ROHN, DR. MED., CARL SCHIRREN, DR. MED., RENATE WEHRMANN, DR. MED., and R. H. O. B. ROBINSON, M.D., F.R.C.S., St. Thomas's Hospital, London. Pp. 337. DM 118.

Vol. XII. *Functional Disturbances.* Prof. ALFRED AUERBACH, University of California, San Francisco; CARL E. BURKLAND, M.D., Sacramento; Prof. GUSTAV-WILHELM PARADE, direktor des Städtischen Krankenhauses Neustadt a.d. Weinstrasse; J. COSBIE ROSS, CH.M., F.R.C.S., Liverpool; DONALD R. SMITH, M.D., Medical School, San Francisco; WALTER W. WILLIAMS, M.D., Springfield, Mass. Pp. 312. DM 98.

TWO new volumes mark continuing progress towards the completion of this major urological work. Volume III, on the investigation of blood, urine, and genital secretions in genitourinary disease, provides much information of fundamental importance to both clinician and pathologist. In an introductory section, which will be particularly appreciated by British readers, Robinson describes the significance of abnormalities of the volume and composition of the urine; and there is a succinct account of the variations of quality of the urine in different forms of urinary disease and its relation to the symptomatology. This section seems all too short and may be in places a little too dogmatic; but it is brilliantly executed and plays an essential part in conditioning the urologist to the accounts of laboratory investigations which form the rest of the volume. They are contributed by several eminent authorities in German, and are detailed and comprehensive. Routine methods of bacteriological and biochemical examinations are supplemented by a description of the various techniques used in hormone estimations and the concentration of antibiotics. A short section is also included on the examination of the prostatic secretion and the ejaculate. This accumulated information will make the volume appeal particularly to those working in laboratories attached to urological departments or clinics; and at the same time it is an essential background to the study of urinary diseases described elsewhere in the *Encyclopædia.*

By contrast, volume XII is essentially clinical and deals with functional disturbances of the genitourinary apparatus. The contributions of five distinguished authors include a general introduction followed by references to such varied topics as neuromuscular dysfunction and paraplegia, urogenital allergy, tetany, and male sterility. With the exception of the section on tetany (in German), all are in English. There is inevitably a little overlap between the introduction and some of the later sections, but each by itself is authoritative and comprehensive. Of outstanding merit is Cosbie Ross' account of neuromuscular dysfunction and paraplegia, containing a great deal of well-illustrated and practical information which those who undertake the care of patients with spinal injuries cannot afford to ignore. Similarly the well-balanced account of the investigation and treatment of male sterility will be of great interest to those engaged in this rapidly expanding area of genitourinary research. Though the title of this volume may be misleading in the sense that "functional" is nowadays frequently misapplied, the contents throughout are highly practical, and make an integral and important contribution to knowledge of urogenital disease.

Protein and Amino Acid Requirements in Early Life

L. EMMETT HOLT, Jr., M.D., department of pediatrics, New York University; PAUL GYÖRGY, M.D., department of pediatrics, University of Pennsylvania; EDWARD L. PRATT, M.D., department of pediatrics, University of Texas; SELMA E. SNYDERMAN, M.D., department of pediatrics, New York University; WILLIAM M. WALLACE, M.D., department of pediatrics, Western Reserve University. New York: University Press. 1960. Pp. 63. $1.

THIS excellent and well-documented monograph sets out clearly and concisely what is known today about protein requirements in early life. Those who know the authors and their contributions to the subject will recognise the parts of the book for which they have been mainly responsible, but the integration has been admirable and the monograph reads perfectly as a whole.

Beginning with the extent to which protein intake may affect the composition of the body, the authors then consider protein requirements at all ages and ways of satisfying them. There is a short section on the quality of protein and the effect of heat on its nutritional value; and the latter part of the book is devoted to the requirements of aminoacids, collectively and individually. The authors discuss the protein requirements, and secondarily the calorie requirements, of people living in undeveloped counties, and summarise the effects, good and bad, which may be anticipated after a large increase in the protein intake. The diagrams and charts are clear and instructive. All interested in infant feeding and in the wider aspects of nutrition should read this book and have it by them.

Man's Posture: Electromyographic Studies

J. JOSEPH, M.D., M.R.C.O.G., reader in anatomy, Guy's Hospital Medical School, London. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960. Pp. 88. 44*s*.

IT has been widely accepted that a man standing upright is held in that position by the " balanced tone " of the several muscles on the back and front of his legs, which, by their opposing action, fix the joints they span. To those who have been taught that some " tone " is present even in muscles at rest, such sustained activity seems not unlikely and only slightly uneconomical; and the fact that no electrical evidence of its existence was forthcoming has been attributed to the difficulty of demonstrating widely separated discharges in an otherwise inert muscle mass.

Dr. Joseph has now shown, by the use of an extremely sensitive electromyograph, that most of the muscles in question are completely relaxed. Only those of the calf, and some in the back, are contracted in the position described, which is otherwise sustained by the strength of the ligaments of the knees and hips. The researches which have led to this conclusion are, in this short monograph, set out in a simple and convincing style which makes it a model for such reporting.

Current Surgical Management

2nd vol. *A Book of Alternative Viewpoints on Controversial Surgical Problems*. Editors: JOHN H. MULHOLLAND, M.D., New York University College of Medicine; EDWIN H. ELLISON, M.D., Marquette University School of Medicine; STANLEY R. FRIESEN, M.D., University of Kansas Medical Centre. Philadelphia and London: W. B. Saunders. 1960. Pp. 348. 56*s*.

SURGICAL opinion is apt to be authoritarian, a conglomerate of tradition and top hat—thus leading to misprision. But there can be no right and no wrong in a subject so full of inexactitudes; indeed, even when other things are equal, a method successful in one man's hands may prove otherwise in another's. That each surgeon should develop his opinions is right; that he should advocate them is understandable; but that too often he espouses them to the exclusion of others is inexcusable. In this second volume the authors pursue their civilising mission by placing side by side contrary opinions on a further selection of important controversial subjects. A topical choice it is too; with repair of hiatus hernia, detection of common-duct stones, treatment of breast cancer, and the significance of large-bowel polyps among the subjects discussed. Many would have welcomed a discussion on the hormonal treatment of breast cancer—the pros and cons of hypophysectomy versus adrenalectomy and the place of androgens and œstrogens—but perhaps this will come in a third volume. As it is, the chapter on breast cancer is confined mainly to the question of radical mastectomy; and the contributor of this chapter kills the recently agreed international method of staging almost before it has been born. This seems to be the one uncivil act in a book in which 50 contributors, who know how to write, have provided much argument for the lunch table at little cost.

Contributions to Obstetrics and Gynæcology

V. N. SHIRODKAR, M.D., F.R.C.S., F.A.C.S., emeritus professor of obstetrics and gynæcology, Grant Medical College, Bombay. Edinburgh: E. & S. Livingstone. 1960. Pp. 159. 37*s*. 6*d*.

Professor Shirodkar is best known in this country for his work on cervical incompetence. The operation which bears his name is beautifully illustrated in the first chapter of this monograph, but the text is disappointingly brief. Very little is said of the results, and no consideration is given to possible complications. There follows a much fuller chapter on prolapse, and a number of criticisms are made of the Manchester-type operation pioneered by Donald and Fothergill. Shirodkar believes that this operation is based upon an imperfect understanding of the ligamentous supports of the uterus, and he describes the modifications which he has introduced. His description is supported by an excellent series of photographs and diagrams. A 95% success-rate is claimed for his operation. For the 5% of failures Shirodkar describes a very elaborate fascial sling operation.

Further chapters are devoted to the surgery of blocked fallopian tubes and to surgical techniques for fashioning an artificial vagina. The remainder of the book consists of summaries of various papers by the author. There is no obvious connection between most of these items, and some are very brief.

French's Index of Differential Diagnosis (8th ed. Bristol: John Wright. 1960. Pp. 1124. 126*s*.).—That this book should be approaching its fiftieth birthday (it first appeared in 1912) is sufficient tribute to the originality of its first author and to its perennial popularity and value as a work of reference. It is still without a rival in its class. The new edition, again ably edited by Dr. A. H. Douthwaite, looks much like its predecessors, but the text has been widely revised and many new illustrations are included. The articles, by 20 hands, maintain the expected high standard, with only very occasional lapses. In the article on incontinence of fæces, for example, no mention is made of fæcal impaction, which must be far commoner than any of the causes mentioned. Incontinence of urine, too, is now such a common condition in an ageing population that it might merit a main article to itself in the next edition. Perhaps that will appear in time to start this unique book on its second half-century of useful life.

The Diabetic ABC (12th ed. London: H. K. Lewis. 1960. Pp. 82. 5*s*. 6*d*.).—In the new edition of this well-known book by Dr. R. D. Lawrence a short section has been included on the use of the sulphonylureas, but phenformin is not mentioned. It is perhaps more of a defect now than formerly that the red portions of the line ration scheme include a set proportion of protein to fat, so that it is hard to vary them independently of each other. This is still possible, however, with this book if the 5-gramme ration scheme is used, although the recipes are not designed for this method. In the soup recipes the amounts of the ingredients are specified without reference to the volume of soup to be prepared. This book has in the past been the mainstay of countless diabetics, and with its wealth of sound practical advice it will preserve that role.

Demographic Yearbook 1959 (11th ed. New York: U.N. Statistical Office. Pp. 719. Clothbound, 71*s*.; paper, 57*s*. Obtainable from H.M. Stationery Office, P.O. Box 569, London, S.E.1.).—The special topic covered is natality statistics from 1949 to 1958. The data show an annual population gain in the world of 48 million. For the first time, an attempt has been made to differentiate the statistics according to their degree of reliability.

THE LANCET

LONDON 26 NOVEMBER 1960

Criminal Justice: 1960

PUBLICATIONS on social subjects have flowed fast of late from H.M. Stationery Office. Within a week or so we have had the reports on Children and Young Persons [1] and on Corporal Punishment,[2] and a draft Bill incorporating many of their conclusions. Such legislative celerity must be almost without parallel. Mr. R. A. BUTLER, the Home Secretary, has left on one side the age-limits of criminal responsibility and provisions for children needing care or protection; partly because they are irrelevant to this Act and partly because he wishes public opinion to form.[3] Much more contentious will be the positive decision not to reintroduce corporal punishment.

The Advisory Council on the Treatment of Offenders, a broadly based body,[4] came to a unanimous conclusion on this after initial disagreement. Their report observes that testimony was notable for its conflicting nature but pays tribute to the medical evidence, saying that " there was far greater unanimity in the views expressed to us by psychiatrists than in those expressed by members of any other profession ". These views, in substance, were accepted by the Council, and some may use anti-psychiatric prejudice to attack the report. But this testimony was a small part of the Council's evidence, and we particularly welcome their extension of the Cadogan Committee's survey [5] of flogged persons (about 3000 altogether) showing that their reconviction-rate was in general slightly higher than where corporal punishment had not been given. It is good, also, to be reminded that the measure favoured by most (flogging for sexual and violent crimes) would put the clock back not twelve years but a hundred and that the present demand for its return is the subject of adverse comment abroad. Certainly it would have been a pity, at a time when the rate of increase of delinquency shows signs of easing, if corporal punishment had been able to claim credit for a spontaneous improvement. It is an interesting commentary on our democratic process to note from the report that the general public, the judges of the Queen's Bench Division, and members of the Magistrates' Association probably favour by significant majorities some form of corporal punishment, but borstal governors and probation officers seem to hold the reverse view (of nine national daily newspapers, incidentally, only the *Express* opposes the Council's conclusions). The will of the people appears this time to have taken second place to dispassionate study of the facts.

The new Criminal Justice Bill proposes, as soon as facilities permit, to exclude nearly all under-21s from prison by making greater use of borstals and detention centres, particularly of the latter. (The provision in the Act of 1948 preventing a lad from going there a second time [6] is to be repeated.) This will mean a change in the character of the detention centres, which will no longer be designed to give a " short, sharp shock " to a restricted group of wayward but physically healthy youths whose disorder is not persistent or deeply ingrained. In fact the intensely disciplined, spartan, and energetic life of the pioneer centres has altered much over the years, and in future we are going to see these centres providing confinement for the young while avoiding the contamination of hardened adult offenders. When the detention-centre network is established, grading of schools and classification of lads (as of prisons and prisoners) will become necessary, though the Act makes no such provision. Notwithstanding magisterial enthusiasm, we have held grave doubts about the effectiveness of " traditional " detention, doubts which were not assuaged by the report of 50% reconviction among these lads within three or four years of discharge.[7] But if the new centres measure up to the best that the Prison Commission have to offer, this part of the Act will be very welcome.

Extension of compulsory aftercare to young people from those centres, and eventually to a wide range of adult prisoners, is valuable and long overdue. Few physicians discharge patients after long-continued inpatient treatment without periodic follow-up and check on progress. What the Act does not take account of is the troubled and inadequate state of existing facilities. The organisation, and the training of suitable staff, will require a good deal of thought.

One of the more surprising proposals in the Act is that any or all of the functions of the Prison Commission may be transferred to the Secretary of State by Order in Council and that ultimately the Commission may be dissolved. It is hard to foresee the implications of this; but, for a time at least, it could mean little more than business as usual behind a different shop front. The Commission, over the past few years, has taken great strides, showing courage in experimenting—or allowing others to experiment—with new ideas. But for hostile public opinion and money troubles, the penal scene could, we believe, have been altered even more. If closer integration with the Home Office stills this independent enterprise and makes the prison service more subservient to political fancy, the move will be tragic indeed. But there is some analogy here with the

1. Report of the Committee on Children and Young Persons. Cmnd. 1191. H.M. Stationery Office. 1960. See *Lancet*, Nov. 5, 1960, p. 1015.
2. Corporal Punishment. Cmnd. 1213. H.M. Stationery Office, 1960. See *Lancet*, Nov. 19, 1960, p. 1149.
3. *Hansard*, Nov. 17, 1960, col. 565.
4. The members were: The Hon. Mr. Justice BARRY, Sir CHARLES CUNNINGHAM, Mr. PAUL BENNETT, Sir GEORGE BENSON, Baroness ELLIOT OF HARWOOD, the BISHOP OF EXETER, Mrs. XENIA FIELD, Mr. B. J. HARTWELL, Mr. J. G. S. HOBSON, The Hon. Lady INSKIP, Mrs. V. CREECH JONES, Mr. J. LEES-JONES, Prof. ALAN MONCRIEFF, Judge Sir BASIL NIELD, Dr. J. D. W. PEARCE, Rev. E. SHIRVELL PRICE, Prof. L. RADZINOWICZ, Mr. R. G. ROBINSON, and Colonel A. E. YOUNG.
5. Report of the Departmental Committee on Corporal Punishment. Cmd. 5684. H.M. Stationery Office, 1938, p. 131.
6. Criminal Justice Act, 1948, section 18.
7. Report of the Commissioners of Prisons for the Year, 1959. Cmnd. 1117. H.M. Stationery Office. See *Lancet*, Nov. 12, 1960, p. 1072.

Board of Control, which retired with honour on Nov. 1 after a century of valuable service (including the earlier period of the Lunacy Commission). The need for day-to-day supervision of mental institutions, essential in the past century, has now gone and their management should resemble that of other hospitals within the N.H.S. Similarly, Mr. BUTLER is evidently looking ahead to a wider organisation covering Home Office responsibilities for criminal justice and the treatment of offenders.[8] Integrated probation, prison, and aftercare services would certainly be welcome.

While one may applaud what is in this Bill, it does not make much progress towards the ultimate goal of a penal system run effectively on factually based concepts of diagnosis and treatment. The conditions for securing accurate knowledge of what prisons do to men are only slowly coming about, and experimental randomising techniques will be fought tooth and nail by the judiciary. But one particularly grotesque gap in our court system could be dealt with in this Act—namely, the complete ignorance of judge or magistrate regarding the outcome for those offenders to whom they give so much thought before taking decisions which make or mar the lives before them. This is like a physician giving a shot of long-acting penicillin to a man with bronchopneumonia without troubling to call again—except that the judge is much less sure that his methods work. Judges, like doctors, need to learn from their errors (and from their successes) and there can be no substitute for the long-term prognostic survey: KRAEPELIN founded psychiatric diagnostics in this way, and there are plenty of hints that penal diagnostics might be similarly elucidated. The new aftercare provisions will help greatly in this, but we believe this Act should be amended by a clause providing that, on expiration of any period of supervision, the original sentencing authority be furnished with a report setting out, in standardised form, the offender's subsequent career with loss of remission and why, participation in the regime, behaviour during aftercare, and so on. Addressed to the clerk of the court (who would forward it if necessary) the report would be followed by supplementary ones, should the man offend again later on. This measure would not only help the courts (and their views on corporal punishment point to the need of that) but would add to the interest of an onerous task and provide a source of research material.

Disorders of Movement

THE functions of the basal ganglia are still a debatable part of neurology. For HUGHLINGS JACKSON the corpus striatum played an important, though somewhat ill-defined, part in the organisation of movement, the lack of definition being illustrated by the fact that he was apt to speak of the neural basis of movements as being situated " close upon " or " on the hemisphere side of " the corpus striatum. KINNIER WILSON's description in 1911 of progressive lenticular degeneration brought part of the corpus striatum into a sharper focus, but also heightened the contrast between the severe and disabling symptoms in man attributed to lenticular degeneration and the physiologist's failure to produce any comparable disorder by experimental lesions in animals. RAMSAY HUNT in 1917 drew attention to the association between degeneration of the globus pallidus and parkinsonism, but within a few years parkinsonism resulting from encephalitis lethargica was to be attributed to degeneration of the substantia nigra. This view later received the support of no less an authority than GREENFIELD. Recently evidence has accumulated that surgical lesions, either of the globus pallidus or of the optic thalamus, may benefit parkinsonism.

Professor DENNY-BROWN's review (concluded in our present issue) is therefore timely; and he is perhaps unique in being able to bring to this complex problem experience in clinical neurology, neuropathology, and neurophysiology. As a clinician he sees the clinical condition of a patient at any particular moment as only a phase in the course of the disorder whose pattern slowly changes through the years. This leads him to recognise resemblances between disorders which, on clinicopathological grounds, have in the past been perhaps too rigidly treated as distinct; or one disorder, which at a certain phase of its evolution appears quite different from another, may at a later stage come to resemble it. As a neuropathologist he seeks to correlate certain clinical pictures with such pathological features as their localisation or diffuseness, acuteness or chronicity. Finally, as a neurophysiologist, he regards disorders of the basal ganglia as producing not merely isolated disturbances of posture, tonus, or movement, but as interfering with the reactions of the organism as a whole to contact and gravity, and as disturbances of its orientation in space of a kind with which the experimental physiologist is familiar in animals. Thus, DENNY-BROWN notes the involuntary movements of Wilson's disease, whether tremulous or athetotic, giving place in time to a hemiplegic posture, a terminal dystonic state which, in his experience, is always present when bilateral rarefaction or frank cavitation of the putamen occurs. In time, however, this gives place to a state of mild general flexion. In Huntington's chorea, too, the earliest involuntary movements pass through an athetoid phase, which again may end in a dystonic state similar to that found in a late stage of Wilson's disease.

DENNY-BROWN's study of the effects of acute lesions of the putamen and globus pallidus is of particular interest. He lays emphasis on the akinetic mute state of general flexion of all limbs, with pronated wrists and extended fingers, that is characteristic of severe damage to the globus pallidus. and in milder cases is associated with tremor of parkinsonian type. In contrast, destruction of the putamen and caudate nucleus leads to rigid flexion of the upper limbs with extension of the lower limbs, greatly intensified by suspending the patient free of contact with body surface. Taking the phenomenon of athetosis as a model, DENNY-BROWN observes that the characteristic elementary postures of athetosis are also encountered in Huntington's chorea and in

8. *Hansard*, Nov. 17, 1960, col. 576.

dystonia musculorum deformans as well as in parkinsonism, in all of which "the essential conflict between proprioceptive inhibition and excitation... is of one degree and not of kind". Hence "plastic rigidity, parkinsonian tremor, and dystonia are different aspects of a conflict of released proprioceptive reactions. The conflict is resolved more slowly in plastic rigidity, more rapidly and rhythmically in tremor, and not at all in intense dystonia."

But these phenomena are to be understood only by taking into account the relations between the basal ganglia and the cerebral cortex. Only when the nervous system is seen as a whole, with the distance receptors conveying information of certain kinds about the environment, while the labyrinths and other proprioceptors as well as the tactile receptors are concerned with more immediate adjustments of the body in response to touch and gravity, can we appreciate the interference produced by lesions of the basal ganglia with these complex interrelations and integrations.

Some Causes of Œdema

METABOLIC studies with ^{131}I-labelled albumin have greatly increased our understanding of the pathogenesis of œdema; and the recognition of massive gastrointestinal protein loss in various digestive disorders has provided clinicians with a new clue to the puzzling syndrome of "idiopathic hypoalbuminæmia."[1–5] Interest in any one mechanism may obscure the fact that usually several abnormalities underlie œdema formation; and a single case studied in great detail by GROSS et al.[6] at the Peter Bent Brigham Hospital, Boston, seems particularly instructive.

The patient was a 59-year-old man with a two-year history of progressive generalised œdema, without either clinical or laboratory evidence of liver, kidney, or cardiovascular disease. Within a few weeks of admission—despite treatment with diet, diuretics, and digitalis—his serum-proteins fell to 2·3 and his serum-albumin to 0·8 g. per 100 ml. The serum was then subjected to a battery of chemical tests, including immunoelectrophoresis on starch-gel, ultracentrifugation, and assay of copper-oxidase activity; and, besides the gross deficiency in albumin, these revealed several abnormalities. The iron-binding γ-globulin fraction and the serum-cæruloplasmin level were decreased; a narrow intensely staining band (with a Svedberg coefficient of 7 units) migrated with the slowest-moving γ-globulins; and a persistently raised serum-cholesterol was associated first with a rise in low-density lipoproteins and later in the disease with an increase in macroglobulins in the α_2-globulin fraction. The Congo-red test and gingival biopsy for amyloidosis were negative; and there was little in the blood-smear or bone-marrow to support the diagnosis of multiple myeloma. The urinary excretion-rates of 17-hydroxycorticosteroids and aldosterone were moderately raised; and turnover studies pointed to increased hydrocortisone synthesis.

Though the patient had no gastrointestinal symptoms, excess fæcal nitrogen excretion (2–8 g. per day) suggested the possibility of plasma-protein leakage into the gut; and, by comparing immunoelectrophoretic patterns, the Boston workers identified four serum fractions in the gastric and duodenal aspirates. This finding, together with lack of sustained response to intravenous albumin and blood-transfusions, justified an exploratory laparotomy; and at operation a thickened, œdematous length of jejunum was resected. (Most of the small gut was engorged, œdematous, and irritable.) The resected segment was tested in vitro for capacity to transport radioactive albumin from its serosal to its mucosal surface—a possible route for plasma-protein loss in the presence of ascites. Though the specimen proved its viability by actively transferring glucose against an osmotic gradient from mucosa to serosa, no reverse shift of albumin was observed. Neither the operation nor a subsequent peritoneojugalar shunt brought any improvement; and the patient eventually died of pulmonary œdema and peritonitis.

The turnover of ^{131}I-labelled albumin[4 7] was twice studied in the course of the illness. If the daily loss in plasma-radioactivity is plotted as a percentage of the radioactivity in the tracer-dose, a curve of two components is obtained. In the first three or four days plasma-radioactivity falls steeply to about 10%—a result mainly of the dilution and equilibration of the injected material in the various body-fluid compartments. A longer-continued and gentler slope represents the breakdown and external loss of the radioactive albumin; and it is from this that the half-life of albumin in the plasma is calculated. It has been shown, however, that even carefully labelled proteins tend to have a shorter half-life than unlabelled material.[8–10] Denaturation accelerates the removal of proteins from the bloodstream; and, before the introduction of new techniques, partial denaturation was the inevitable side-effect of over-iodination, heat-treatment for sterilisation, and internal radiation damage.[11 12] Nevertheless, comparison of the half-lives of identical preparations of ^{131}I-albumin in the patient and in healthy controls showed that albumin disappeared from the patient's plasma about twice as fast as from the plasma of the controls; and calculations based on this finding indicated that his fractional rate of albumin catabolism was considerably increased. Such an increase does not necessarily mean that abnormally large amounts of albumin are broken down. Obeying the law of first-order reactions, albumin catabolism removes a more or less fixed proportion of the total body pool each day, not a fixed number of molecules [8]: and the fractional rate of turnover is therefore increased when the body pool is reduced more than the breakdown-rate (as can happen in cirrhosis or proteinuria); and, conversely, it declines when the body pool is increased disproportionately to a rise in albumin synthesis. It is, of course, far from easy to measure with any accuracy the albumin pool of a patient with gross œdema,

1. Albright, F., Bartter, F. C., Forbes, A. P. *Trans. Ass. Amer. Phycns*, 1949, **62**, 204.
2. Schwartz, M., Jarnum, S. *Lancet*, 1959, i, 327.
3. Young, W. F., Levin, B., Fowler, J. F., Miles, J. M. *ibid.* 1959, ii, 85.
4. *Lancet*, 1958, ii, 1000.
5. *ibid.* 1959, i, 14.
6. Gross, P. A. M., Laurence, J. E., Bally, P., Shipp, J. C., Thorn, G. W. *Amer. J. Med.* 1960, **29**, 386.
7. Gitlin, D., Janeway, C. A., Farr, L. E. *J. clin. Invest.* 1956, **35**, 44.
8. Gitlin, D. *Pediatrics*, 1957, **19**, 657.
9. Bennhold, H., Kalee, E. *J. clin. Invest.* 1959, **38**, 863.
10. Freeman, T., Matthews, C. M. E., McFarlane, A. S. *Nature, Lond.* 1959, **183**, 606.
11. McFarlane, A. S. *Biochem. J.* 1956, **35**, 746.
12. Hayter, C. J. *J. clin. Path.* 1960, **13**, 369.

effusions, and ascites; but qualitatively if not quantitatively the estimates of GROSS et al. can be accepted. These showed that their patient catabolised only 9 g. albumin per day (the normal range is 15–25 g.), but that this figure represented 13·1% of his total body pool (normal 4–6%). The state in this case contrasts strikingly with that in congenital analbuminæmia, which Professor BENNHOLD and his colleagues discuss in their article on p. 1169.

In the absence of external loss in the urine or fæces, or from exudative skin lesions, an increased fractional rate of albumin catabolism points to excessive albumin breakdown in the tissues or to albumin exudation and breakdown in the gastrointestinal tract. Neither of these processes is easily measured. Since the stomach excretes a considerable amount of $H^{131}I$ (in place of HCl) estimations of total ^{131}I activity in the gastroduodenal juices and in the fæces are of little significance; and rapid breakdown of labelled albumin by intestinal enzymes and reabsorption of the aminoacid residues, including ^{131}I-tyrosine, interfere with the measurement of albumin-bound ^{131}I. (Labelled polyvinyl pyrrolidine, recently introduced by GORDON,[4 13] overcomes this difficulty: it has a similar molecular weight to that of albumin but it is not hydrolysed by gastrointestinal enzymes.) Another difficulty lies in our ignorance of where albumin is normally catabolised in the body. Experimental work strongly suggests that the reticuloendothelial system plays a dominant part [14 15]; but in the Boston case attempts to inhibit reticuloendothelial-system activity by various forms of steroid therapy [16] were ineffective.

Though a raised fractional rate of albumin catabolism alone can account for hypoalbuminæmia, other mechanisms must probably operate before œdema develops. The grossly subnormal rate of albumin synthesis (9 g. per day) in the patient investigated by GROSS et al. is the more surprising since in many hypercatabolic states the body can balance increased loss by an increase in albumin synthesis. Albumin, moreover, is synthesised entirely by the liver; and not only did liver-function tests fail to reveal signs of parenchymatous damage but postmortem examination also showed that the liver was relatively healthy. Albumin hypoanabolism, however, is occasionally the sole manifestation of liver dysfunction—another reminder that, unless interpreted with great caution, " liver-function " tests can be as meaningless as body-function tests.

A third abnormality which undoubtedly contributed to œdema formation was increased capillary permeability, leading to an increase in the extravascular colloid-osmotic pressure.[17] The normal interstitial-fluid volume is about three times the plasma-volume; and, though it cannot be directly sampled, studies with ^{131}I-labelled albumin suggest that it contains about half the total body albumin.[18] With œdema, effusions, and ascites, the interstitial-fluid volume may double or triple; and, since in most œdematous states the percentage-distribution of albumin between the fluid compartments remains the same, the interstitial-fluid albumin concentration usually falls. (In the nephrotic syndrome it may fall to a hundredth of the serum concentration.) In the Boston case, by contrast, it remained about a third of the serum concentration throughout the illness and several observations suggested that this could be accounted for by albumin leakage through the capillary walls. The initial studies of ^{131}I-labelled-albumin turnover showed an abnormally brisk diffusion of the injected material; and intramuscular growth-hormone—given in the hope that it might stimulate connective-tissue formation and diminish capillary permeability [19 20]—resulted in an even more dramatic shift in the reverse direction. Though the treatment lost its effectiveness after twenty-four hours, for a brief period the patient's serum-albumin rose from 1·3 to 5·1 g. per 100 ml., his serum concentration of labelled albumin increased fourfold, his serum-cæruloplasmin level doubled, and dilated submucosal lymphatics were observed in œdematous areas.

GROSS et al. conclude their important study by noting that their patient, besides a greatly diminished total albumin pool, showed extreme muscular wasting. This was further evidence for WHIPPLE's thesis [21] that protein metabolism must be assessed in terms of a dynamic equilibrium between the intravascular, interstitial, and tissue proteins.

Infection by Anonymous Mycobacteria

THE relative importance attached to clinical, radiological, and bacteriological criteria in the diagnosis of pulmonary tuberculosis has varied at different times and in different circumstances. A by-product of closer attention to bacteriological findings has been the recognition of lung infections masquerading as tuberculosis but caused by mycobacteria quite distinct from tubercle bacilli—infections which we termed " mycobacterial pseudotuberculosis ".[22 23]

The name " anonymous mycobacteria " has been given to mycobacteria, isolated from human morbid material, which are distinct from tubercle bacilli and other accepted species. So defined, the group contains mycobacteria of undoubted pathogenicity and also casual transient intruders. Pathogenic strains cannot be identified with certainty by their properties, but a mycobacterium isolated repeatedly in the absence of any other evident cause may be regarded as a presumptive pathogen. Casual anonymous strains are rarely isolated more than once from any one patient. Classification of the anonymous mycobacteria owes most to RUNYON,[24] who has defined the following groups:

1. Photochromogens, which are cream or buff in the dark but produce a yellow or orange pigment rapidly after exposure to light.

13. Gordon, R. S., Jr. *Lancet*, 1959, i, 325.
14. Gitlin, D., Klinenberg, J. R., Hughes, W. L. *Nature, Lond.* 1958, **181**, 1064.
15. Katz, J., Rosenfeld, S., Sellers, A. L. *Fed. Proc.* 1959, **18**, 257.
16. Rotschild, M. A., Schreiber, S. S., Oratz, M., McGee, H. L. *J. clin. Invest.* 1958, **37**, 1229.
17. *Lancet*, Oct. 1, 1960, p. 746.
18. Veall, N., Vetter, H. Radioisotope Techniques in Clinical Research and Diagnosis. London, 1958.
19. Scow, R. O. *Endocrinology*, 1951, **49**, 641.
20. Wegelius, O., Ashoe-Hansen, G. *Acta endocr., Kbh.* 1956, **49**, 641.
21. Whipple, G. H. The Dynamic Equilibrium of Body Proteins. Springfield, Ill., 1956.
22. *Lancet*, 1955, ii, 758.
23. *ibid.* 1959, i, 1266.
24. Runyon, E. H. *Med. Clin. N. Amer.* 1959, **43**, 273.

2. Scotochromogens, which are yellow, orange, or reddish from the start of growth both in light and in dark.

3. Non-photochromogens, which are cream or buff grown in the light or in the dark, although some strains slowly become yellow or reddish.

RUNYON distinguishes rapidly growing non-photochromogens as group 4, but opinions differ on this separation. Photochromogens, for which the name *Myco. kansasii* has been proposed, are a homogeneous group with limited but definite pathogenicity for laboratory animals; in man they seem usually to be pathogenic. In contrast, scotochromogens are almost always casual intruders without significance. Non-photochromogens are a heterogeneous group which at present cannot be satisfactorily subdivided; they include both pathogenic and casual strains, the relative proportions varying between different areas.

LEWIS et al.[25] report from Florida 116 cases of pseudotuberculosis due to non-photochromogens. The organism was demonstrated repeatedly by culture in all cases and by smear in 70%. Symptoms were similar to those of tuberculosis and included cough, loss of weight, low fever, and, in some cases, hæmoptysis. Radiological appearances were indistinguishable from those of tuberculosis, and cavitation was present in 78%. Skin tests with standard P.P.D. and a protein preparation from a non-photochromogen culture were made in 50 cases and were compared with the results in 50 cases of tuberculosis. In the great majority there was a larger reaction to the homologous antigen. A disquieting feature of the study was that patients with pseudotuberculosis fared less well than those with tuberculosis. The cause was no doubt the inherent resistance of non-photochromogens to most chemotherapeutic agents (photochromogens are somewhat less drug-resistant), though a fair number of strains were sensitive in vitro to viomycin, cycloserine, kanamycin, and streptovaricin. Of a total of 78 patients treated medically, 15 died, 44 were considered still to have active disease on discharge from hospital (27 remaining bacteriologically positive), and only 19 appeared to have overcome their infection. Resection was undertaken in 37 cases and plombage in 1. Complications of surgery were rather commoner than in tuberculosis; they included bronchopleural fistula in 3 cases and hæmorrhage in 2. In 2 cases death followed operation. The disease became inactive in 30 patients.

Experience in Florida, as in this country, suggests that in many cases of pseudotuberculosis resistance to mycobacterial infection has previously been lowered by other chest disease or by debilitating conditions such as alcoholism or gastric resection. Occasional cases in patients on steroid therapy suggest that this, too, may predispose to the infection. The incidence of anonymous mycobacteria in Florida is similar to that reported for Wales by MARKS and TROLLOPE,[26] who found these organisms in 2% of new patients yielding mycobacteria on sputum culture; but only 42% of their anonymous strains were judged to be pathogenic.

25. Lewis, A. G., Lasché, E. M., Armstrong, A. L., Dunbar, F. P. *Ann. intern. Med.* 1960, **53**, 273.
26. Marks, J., Trollope, D. R. *Tubercle, Lond.* 1960, **41**, 51.

Our previous suggestion that patients with pseudotuberculosis should not be treated in contact with cases of tuberculosis is supported by the observation in Florida that 2 such patients acquired infection with drug-resistant tubercle bacilli in hospital. In contrast, healthy contacts of patients with pseudotuberculosis do not seem to be at risk. The early diagnosis of mycobacterial pseudotuberculosis is important; for delay may jeopardise the success of surgery, which in many cases offers the best hope of cure. Recognition of the disease depends chiefly on bacteriology; and a routine method of screening mycobacteria, such as that recommended by MARKS and TROLLOPE, is a necessity in diagnostic work. The clinician should consider the possibility of pseudotuberculosis particularly in men over 40 who react poorly to anti-tuberculosis treatment and in patients predisposed to the infection by pneumoconiosis or debilitating disease.

Annotations

THE MEDICAL ADVISER

"LET me introduce you to my medical adviser", people sometimes say; and in his James Mackenzie lecture to the College of General Practitioners last Saturday Dr. Lindsey Batten talked about the doctor's role as adviser to his patients. The doctors of Dr. Batten's vintage had on the whole a very creditable medical education, with an eye to general practice; but, even so, he said, they were not taught the art of advising or urged to look forward to it as an important part of practice.

Taking examples from the various ages of man, Dr. Batten spoke of questions about heritable disease and marriage as illustrating his view that the doctor's job is "to advise, not to give orders or pass judgment". In pregnancy "the personal medical adviser is at least as much needed in these days of antenatal clinics and books and pamphlets for expectant mothers as he was before they existed"; for somebody must be prepared to listen, explain, and advise, even if only for "the odd person who wants to know". Infant welfare—a province hard but not impossible for the practitioner to regain—carries the same need for something more than standardised advice: the young mother up against infant perversities and conflicting counsel can be greatly helped by someone with quite a small fund of apposite knowledge who is not blown about by every wind of doctrine. And it is the same with toddlers, with their variations on a nursery theme.

"'Not use my pot', 'not eat my dinner', 'not go to sleep' comprise the whole thematic material—it could even be shortened to 'not'; but so fertile are they in invention, so adept in the devices of augmentation, inversion, and ornament that every mother believes her particular little fiend to be playing a new tune."

After touching on sexual instruction—part of which can very well come from the family medical adviser—and the advantage for boys and girls to feel that they have an unshockable medical friend, Dr. Batten turned to invalidism of the form of disability too often called chronic neurosis. Needless "distrust of a vital organ" can easily be sown and grow, and though its uprooting may require a consultant as well as a family doctor, it is a personal task for which teams and institutions are wholly unfitted. If a young man thinks his heart is at fault, the

last kind of specialist he will see is a psychiatrist; and often only the personal doctor has a chance of giving the help needed.

Reasons may be plentiful, but the hard fact remains that time and again the patient returns from hospital or consulting-room with questions unanswered or unasked and dark speeches unilluminated or misapprehended. Once again there is only one possible source of light—the personal medical adviser. Were he to disappear

"there would be no public outcry for his re-establishment and the Ministry would not notice the difference. The fragmentation of medicine, the adulation of teamwork, the curious belief that uniformity is somehow identical with justice, the unquestionable fact that he is, as they say, 'uneconomic'—all these militate against him. His chances seem poor and yet if he goes the sum of human unhappiness, great enough already, will be greater and the satisfaction of medical practice to the practitioner will be less".

To save him, Dr. Batten said, two things are needed. First we must keep his image bright before the eyes of all concerned, and secondly we must not rest until we secure for him the one indispensable requirement—time. Time to listen, to think, and to talk.

ADENOVIRUS VACCINATION

SOME adenoviruses (notably types 3, 4, 7, and 14) are known to cause serious epidemics of respiratory diseases, mainly among military recruits and children. The early studies were carried out in America, but adenoviruses have been shown to be important in this country among R.A.F. recruits and public-school boys.[1–4] Bell et al.[5] found in volunteers that protection against the disease was conferred by antibody. Two groups in America, led by Huebner [6] and Hilleman,[7] who were the two discoverers of this group of viruses, have shown that a formalin-inactivated vaccine containing either one type or the three most prevalent epidemic types (3, 4, and 7) confers protection against these infections by producing a specific antibody response. The vaccines were prepared from adenoviruses grown on cultures of monkey-kidney cells in a similar way to that used for poliovaccine manufacture. The importance of adequately inactivating the virus was indicated by Hilleman et al.,[8] who inoculated volunteers with living virus and produced respiratory symptoms with conjunctivitis.

Hitchcock and her colleagues [9] have now shown that satisfactory antibody responses can be achieved with low doses of attenuated adenoviruses, probably without producing symptoms They used strains of adenovirus types 4 and 7 adapted to grow in pig-kidney cells.[10] The type-4 virus had had 11 passages in pig-kidney cells and the type 7 either 7 or 17 passages. 13 volunteers were given type-7 virus, and in the 4 without detectable neutralising antibodies to type 7 these developed as a result of vaccination; of these 4, 2 received only 150 T.C.D.$_{50}$ intranasally. In 3 volunteers who received 250 T.C.D.$_{50}$ of type-4 virus no neutralising antibodies developed, but in 2 who received 2500 T.C.D.$_{50}$ antibodies did develop. Some of those who received type-7 virus also showed a rise in titre against type-3 virus if they already had some antibody to type 3.

In some who received the attenuated adenovirus mild symptoms developed; several of these showed no serological evidence of adenovirus infection, and since the trials coincided with an unusually high incidence of mild coryza with slight abdominal symptoms even in control volunteers, Hitchcock et al. were uncertain that the symptoms were due to the adenovirus vaccine. In 6 of the 8 people with serological evidence of infection with type-7 virus, this was isolated either from throat swabs or from fæces; but the virus was not present in very large amounts, and it could be transmitted only with difficulty from man to man.

This work suggests that attenuated living adenovirus vaccine may be a practicable, cheap, and easy means of conferring resistance to adenovirus infections. Larger-scale trials in susceptible child or recruit populations would be necessary in order to show that the method prevents epidemic adenovirus disease. If it is effective its use might be considered not only in susceptible school or recruit groups but also for infants, in the hope that a significant amount of respiratory-virus infection would be prevented. Respiratory infections, not all of course due to adenovirus, account for nearly 50% of all illnesses in children under 5.[11]

HYSTERIA: SYMPTOM OR DISEASE?

HYSTERIA, that most venerable of psychiatric syndromes, seemed, by the classic studies of hypnosis and dissociation, to be one of the most firmly founded entities. Low concordance of diagnosis between physicians, however, and the frequent discovery of other disease underlying the dissociated state has weakened the concept; and Dr. Eliot Slater, in a Maudsley lecture, delivered in London on Nov. 18, cast the severest doubt on hysteria as a "disease".

From the basic hypothesis that monozygotic twins offered a controlled study set up by Nature, Dr. Slater had constructed a survey of hysteria. 12 each of monozygotic and dizygotic twins with a diagnosis of "Hysteria, code number 311" had been collected from cases seen at the Maudsley and Belmont Hospitals. Not one single twin partner of either group had received a formal diagnosis of hysteria—a concordance of 0%, which, even including a doubtful case, seemed to rule out a genetic background. Widening the comparison to other neuroses and to cases treated by the general practitioner brought in several twin-pairs but did not lend support to a genetic hypothesis. Study of the family history brought to light no single secondary case of hysteria among parents and siblings, and no excess of psychiatric disorder of any kind except manic-depressive illness.

As to the effects of environment, affected dizygotic twins were found to be at birth significantly lighter, and in youth poorer in health, than their partners. A preponderance of left-handedness and ambidexterousness in affected twins also suggested a physical basis in some cases. Many other early factors—parental attitude, birth order, feeding difficulties, &c.—were not significantly different between the twin partners. Adult bodily health,

1. Tyrrell, D. A. J., Balducci, D., Zaiman, T. E. *Lancet*, 1956, ii, 1326.
2. Kendall, E. J. C., Riddle, R. W., Tuck, H. A., Rodan, K. S., Andrews, B. E., McDonald, J. C. *Brit. med. J.* 1957, ii, 131.
3. McDonald, J. C., Wilson, J. S., Thorburn, W. B., Holland, W. W., Andrews, B. E. *ibid.* 1958, ii, 721.
4. Munro-Ashman, D., Gardner, P. S., Taylor, C. E. D., McDonald, J. C. *Lancet*, 1958, ii, 121.
5. Bell, J. A., Ward, T. G., Huebner, R. J., Rowe, W. P., Suskind, R. G., Paffenbarger, R. S., Jr. *Amer. J. publ. Hlth*, 1956, **46**, 1130.
6. Bell, J. A., Hantover, M. J., Huebner, R. J., Loosli, C. G. *J. Amer. med. Ass.* 1956, **161**, 1521.
7. Stallones, R. A., Hilleman, M. R., Gauld, R. L., Warfield, M. S., Anderson, S. A. *ibid.* 1957, **163**, 9.
8. Hilleman, M. R., Hodges, R. E., Warfield, M. S., Anderson, S. A. *J. clin. Invest.* 1957, **36**, 1072.
9. Hitchcock, G., Tyrrell, D. A. J., Bynoe, M. L. *J. Hyg., Camb.* 1960, **58**, 277.
10. Guerin, L. F., Guerin, M. M. *Proc. Soc. exp. Biol., N.Y.* 1957, **96**, 322.
11. Miller, F. W. J., Court, S. D. M., Walton, W. S., Knox, E. G. Growing Up in Newcastle upon Tyne. London, 1960.

however, was considerably poorer in affected twins and might provide a background for hypochrondriacal preoccupations.

Turning to the incidence of other disorders in this group of twins, Dr. Slater noted an excess of epilepsy, schizophrenia, endogenous depression, and especially personality disorder characterised by abnormal tension and anxiety, or timidity and shyness. The sexual histories of most cases were full of problems and marital maladjustment. Historical search for psychogenesis was unrewarding in half, and the stresses precipitating the hysterical episodes in most others were often trivial. Prognosis, over some five to seven years, was surprisingly varied, and poorer than was often thought; more than half still had symptoms. It seemed that disappearance from psychiatric clinics of the young hysteric was due more to disappointment than to remission. Cosseting by the marital partner was associated with a lengthy illness.

Dr. Slater remarked that the feature emerging most strongly from his study was heterogeneity. Heredity, history, diagnosis, personality, response to treatment, and outcome varied so greatly among hysterics that he doubted the existence of the condition as an entity. Just as Ganser states and anorexia nervosa were thought to occur in different conditions, so, he suggested, hysterical phenomena of a more general kind were to be regarded as symptoms that might have arisen from a variety of causes. Hysteria was often diagnosed where the case was obscure or treatment failed: histrionic elements, lack of genuineness, or demand for (rather than acceptance of) treatment all led to this diagnosis—one which was often made in no state of emotional detachment, and one which probably indicated that the physician had not looked deeply enough.

THE CASE AGAINST TRENDELENBURG'S POSITION

THE " head-low " position described by Trendelenburg seventy years ago [1] is still widely used as an aid to pelvic surgery, but the circumstances which led to its introduction have changed, and whether there is any need for this position in modern surgical practice is debatable. Abdominal relaxation was difficult to achieve in Trendelenburg's day; and only by lowering the patient's head and applying several abdominal packs could the surgeon keep the intestines out of the pelvic operating field. With modern anæsthesia, including relaxants, the same operative exposure can be achieved with the patient in the horizontal position.

Swain [2] believes that the Trendelenburg position accounts for many cases of postoperative shock, lobar collapse, pneumonia, and venous thrombosis. Impressed by the seriousness of these complications he has stopped using the position in his theatre. In 100 consecutive pelvic operations with the patients lying flat he has achieved excellent accessibility and visibility of the pelvic organs, and postoperative complications have ceased to be a problem on his unit. Most anæsthetists will applaud Swain's initiative; for they have long been concerned over the related embarrassment to cardiovascular and respiratory systems, particularly in obese and hypertensive patients. It remains to be seen whether Swain's suggestion finds favour with gynæcologists, most of whom have been trained to operate with the patient in the Trendelenburg position.

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FOOT-AND-MOUTH DISEASE

FOOT-AND-MOUTH disease, which affects pigs, sheep, and goats as well as cattle, has an incubation period of 3-5 days and is spread by droplet infection, by direct contact, or by contaminated objects. Almost anything which moves or can be moved from one farm to another may spread this highly communicable virus, which multiplies very rapidly in the tongue epithelium, in blisters round the mouth, or in bulbs of infected animals' heels. Outbreaks in this country arise from virus imported either from nearby endemic areas in the Low Countries or France, or by contaminated meat from South America. The present outbreak began at a time when huge flocks of starlings and other migratory birds cross the North Sea to winter here, but there is no evidence that they started the trouble. Workers at the Foot and Mouth Research Institute at Pirbright are convinced that the virus remains infective on the feet, feathers, and droppings of starlings for many hours, but it is, of course, virtually impossible to incriminate birds in a particular outbreak. Previous epidemics here have often followed explosive outbreaks on the Continent, but this year there has been no topping-up in the neighbouring reservoirs and in any case there seems to have been only one primary focus in this country. Evidence from this focus was very scanty, but it is widely believed that infected meat from South America found its way unboiled into pig swill, and from pigs other stock were infected. This is the other main route of spread, and farmers, possibly with other considerations also in mind, naturally emphasise these controllable sources of infection. Last week the Government met some of their requests, and from Feb. 1 next year imports of pork and pig offal, which are said to be inadequately inspected at the South American ports, will be prohibited.

Veterinary investigation officers of the Ministry of Agriculture have already untangled much of the revealing story of the present outbreak. Infected cattle from the north of England were sent to be sold at Stowmarket and later arrived in Diss and then at Norwich market, which soon became the main centre of spread in England. Scotland is often spared these outbreaks; but cattle from Newcastle, sent in error to Norwich before reaching their true destination in Aberdeen, contaminated the market pens and spread the disease widely through the North-east and as far as Glasgow and the Orkney Islands. Although nothing of the sort has yet happened, conceivably the greatly increased herds of wild deer in Scotland may one day acquire the infection and become a more serious and more persistent menace than hedgehogs, the only other wild animal susceptible to the virus. By the end of last week there had been outbreaks in nearly 150 farms and markets, and already this will cost £500,000 in compensation. In the last major epidemic in 1951–52 there were about 600 outbreaks requiring the slaughter of 85,000 animals, and it is interesting to recall that subsequent investigations showed that half the outbreaks could be traced to a single incident near Crewe.

So far this year there has been little open criticism of the policy of slaughtering all infected animals and their contacts, and farmers are to be congratulated on their attitude to this harsh but essential measure. Present-day vaccines are not a reasonable alternative: an effective vaccine must cope with the many antigenic types of virus—the older types O, A, and C, plus 3 South African and 1 Asian strain —and provides an immunity after vaccination which is both type-specific and comparatively shortlived. Though newer

vaccines are being tried in South Africa, it is from the investigations at Pirbright and elsewhere that progress is most likely to come. Since Brooksby's review [1] of recent knowledge of the virus, much fundamental information has come to light, and recently Bradish et al.[2] studied the antigens concerned in complement-fixation tests, which are of great importance since they provide the only qualitative procedure sufficiently sensitive for the investigation of field and experimental samples. Two main components are concerned: one is infectious, type-specific, and about 25 mμ wide; the other, 7–11 mμ, is non-infectious, and has only disease-group specificity. Bachrach,[3] comparing complete virus with the infectious nucleic acid, has shown by the tissue-culture plaque technique that single ribo-nucleic-acid molecules rather than clumps seem to be the infectious units when tested on cultures of calf-kidney. But these important investigations are cold comfort for the farmer, who is concerned with an effective vaccine or other means of dealing with the endemic pools of infection which constantly threaten to spill over into the few fortunate areas of the world where virus-free stock can be raised. Meanwhile, slaughter remains the only practical policy, and the apprehensive farmer behind his antiseptic moat is as effectively isolated as the Weston neighbours of Parson Woodforde when smallpox made visitation on his parish nearly two hundred years ago.

VIRAL DISEASE OF THE CENTRAL NERVOUS SYSTEM

ASEPTIC meningitis, which would formerly have been diagnosed usually as non-paralytic poliomyelitis, is now known to be often due to organisms other than polioviruses. In the first trial of killed poliovaccine [4] the vaccine proved relatively ineffective against "non-paralytic poliomyelitis". This, as Lennette et al.[5] have clearly shown, was not because vaccine is ineffective against non-paralytic poliomyelitis, but because most cases of aseptic meningitis with this clinical diagnosis are not due to poliovirus. Subsequent extensive studies of three viral diseases of the central nervous system—paralytic poliomyelitis, encephalitis, and aseptic meningitis—have shown that some cases of all three syndromes are not due to poliovirus. Although poliovirus is a well-recognised cause of encephalitis [6] it has long been known that other viruses are more usual causes. In Lennette's [5] investigation, for example, although a viral diagnosis was made in only just over 20% of the cases, of those diagnosed 15% were due to Coxsackie viruses, 12% to mumps, 7% to herpes simplex, and 5% to poliovirus. In a larger study Meyer et al.[7] made a specific diagnosis in 72% of cases with a diagnosis of encephalitis. 22% were due to mumps virus, 20% to lymphocytic choriomeningitis, 20% to arthropod-borne viruses, 13% to herpes simplex, 5% to poliovirus, and 5% to other enteroviruses. In this study an ætiological diagnosis was made in 81% of the cases of paralytic poliomyelitis. 113 cases were due to poliovirus and 1 each to mumps, a Coxsackie B, and an Echo virus. In Lennette's [5] study 24% of the vaccinated paralytic cases in which the ætiology was determined were due to poliovirus (the figure was 70% for the non-vaccinated), 17% were due to Coxsackie or Echo viruses, 5% to mumps virus, and 3% to herpes simplex. Lennette et al.[8] describe in detail 11 cases of mild paralytic "poliomyelitis" due to mumps virus. All these patients recovered well, although 2 had mild residual weakness when examined two to five months after onset. It is thus clear that mumps virus can cause encephalitis, lower-motor-neurone paralysis, and aseptic meningitis. In Meyer et al.'s [7] study of the 71% of cases of aseptic meningitis in which an ætiological diagnosis was achieved about 23% were due to mumps virus and 13% to poliovirus. McLean et al.[9] in 1959–60 isolated mumps virus from the cerebrospinal fluid of 17 out of 42 patients with aseptic meningitis thought likely to be due to mumps. In all, 56 cases were studied, and by virus isolation or serology 38 were shown to be due to mumps.

It is now clear that several members of the enterovirus family besides poliovirus can occasionally cause mild paralytic poliomyelitis.[10] Grist [11] has shown that in the Glasgow area in the summer of 1959 Coxsackie A7 caused a significant number of cases of paralytic poliomyelitis, including 1 death. It seems certain that the relative frequency of these cases not due to poliovirus will increase in the next few years as the vaccination programme makes its impact felt. In Northern Ireland Likar and Dane [12] have found that some cases suspected of being paralytic poliomyelitis are due to Russian spring-summer encephalitis or louping-ill virus.

The ætiology of aseptic meningitis is varied and alters from year to year.[13] Meyer et al.[7] succeeded in making an ætiological diagnosis in 71% of cases; but the 45% of Lennette's [5] investigation is perhaps more representative of usual experience. One reason for the relatively low recovery-rate of viruses in these cases may be that the methods of viral isolation are still inadequate despite all the recent improvements. This is suggested by a study by Duncan [14] in which a new Echo virus (Frater), responsible for many cases of aseptic meningitis, was isolated much more frequently in human thyroid cells than in the more commonly used monkey-kidney or human amnion cells. Grist [11] showed the importance of supplementing tissue-culture methods by the inoculation of suckling mice, since the Coxsackie A7 strains he studied did not grow in the commonly used tissue-culture cells. Similarly, the high rate of ætiological diagnosis achieved by Meyer et al.[7] involved not only isolation of viruses but also a battery of serological tests on acute and convalescent sera to cover a wider range of possible ætiological agents. Similarly, as McLean et al.[9] showed, it is important to examine not only fæces but also cerebrospinal fluid if non-enteroviral viruses causing encephalitis, paralytic disease, or aseptic meningitis are to be recovered.

Dr. G. F. ABERCROMBIE has been re-elected president of the College of General Practitioners.

Dr. N. M. GOODMAN, a principal medical officer of the Ministry of Health, has been appointed a deputy chief medical officer of the Ministry in succession to Dr. G. E. Godber who, as already announced, becomes chief medical officer on Dec. 1.

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Public Health

100% SPUTUM-CONVERSION IN NEWLY DIAGNOSED PULMONARY TUBERCULOSIS

H. E. THOMAS, M.D. Lond., M.R.C.P.
D. E. P. FORBES, M.D. Edin., M.R.C.P.E.
G. R. W. N. LUNTZ, M.R.C.P.
H. J. T. ROSS, M.R.C.P.E.
J. MORRISON SMITH, M.D. Glasg., M.R.C.P.E., D.P.H., D.T.M. & H., T.D.D.
V. H. SPRINGETT, M.D. Lond., M.R.C.P.
From the Birmingham Chest Service

"THE right use of modern methods of chemotherapy now makes it possible to aim at 100% success in the treatment of pulmonary tuberculosis." This is the opening sentence of the paper by Crofton (1959) in which he presents an analysis of 240 patients whose bacilli were sensitive to at least two of the three main anti-tuberculosis drugs, all of whom became sputum negative under his regime. As we know of no other survey showing similar results we decided to investigate the results achieved in the Birmingham chest hospitals.

Patients are admitted to one of the three Birmingham chest hospitals from the Birmingham Chest Clinic and all bacteriological and resistance tests are done in a single laboratory. Resistance testing was first employed towards the end of 1955; but examination of cases at diagnosis, did not become a routine practice in all hospitals until about the middle of 1956. We therefore decided to investigate sputum conversion in all patients admitted to the Birmingham hospitals between Jan. 1, 1957, and Dec. 31, 1958.

Of 1770 cases notified in Birmingham as suffering from respiratory tuberculosis in this period, 264 were children of 14 years of age or less. It is estimated that about 200 cases were notified to and treated in other hospitals in this city. Of cases newly diagnosed at the chest clinic, it was not possible to admit all the patients to one of our three chest hospitals and beds were found elsewhere for 157 cases. We judge that about 100 notified cases were also treated at home. Thus about 1000 newly diagnosed cases of respiratory tuberculosis were admitted to the Birmingham chest hospitals.

From all these, cases were selected which had bacteriological specimens which were positive on culture for tubercle bacilli, enabling resistance tests to be done. Whereas normally the resistance test was done on admission, a case was included if the only specimen from which a sensitivity test was made was produced up to two months before or after admission. (Thus a patient would be included because a positive culture was obtained up to two months before admission yet no positive culture was found in any specimens taken on admission.) Again it was necessary for the patient to be cooperative and premature discharge from hospital against medical advice caused the case to be excluded.

The method of drug-resistance testing was that described by Thomas (1960) using for isoniazid the method of the Medical Research Council (1953), for *p*-aminosalicylic acid (P.A.S.) the method of Mitchison and Monk (1955), and for streptomycin, the method of Stewart (1955). An organism was considered resistant if twenty colonies or more grew at 28 days on a concentration of 1 μg. or more of isoniazid per 100 ml., on 2 μg. or more of P.A.S., and on 3 μg. or more of streptomycin.

As all culturally proved cases admitted had the resistance tests performed, it is possible to calculate the incidence of primary drug resistance in accordance with the above definition during this two-year period.

Results

545 newly diagnosed patients with pulmonary tuberculosis admitted to the three chest hospitals had positive bacteriological tests from which resistance tests were made. The results are shown in table I. This gives an incidence of primary drug resistance in this series from the city of Birmingham of 3·1%, of which 2·6% is resistance to one drug and 0·5% resistance to two drugs. Resistance to streptomycin accounts for about half of the total and resistance to isoniazid and P.A.S. for the remainder.

In estimating the percentage of cases showing sputum conversion according to the criteria of Crofton (1958), the

TABLE I—INCIDENCE OF DRUG RESISTANCE AT DIAGNOSIS

Sensitivity	Cases
Sensitive to all three drugs	528 (*96·9%*)
Resistant to isoniazid only	3 (*0·5%*)
Resistant to P.A.S. only	3 (*0·5%*)
Resistant to streptomycin only	8 (*1·5%*)
Resistant to isoniazid and streptomycin	2 (*0·4%*)
Resistant to isoniazid and P.A.S.	1 (*0·2%*)
Total	545 (*100%*)

3 cases with resistance to two drugs are excluded. In this series of patients 12 died within eight months and are also excluded. These cases fall into two groups. In the first (5 patients) all died of acute pulmonary tuberculosis within one month of admission to hospital. In the second group (7 patients), all died of a disease other than pulmonary tuberculosis.

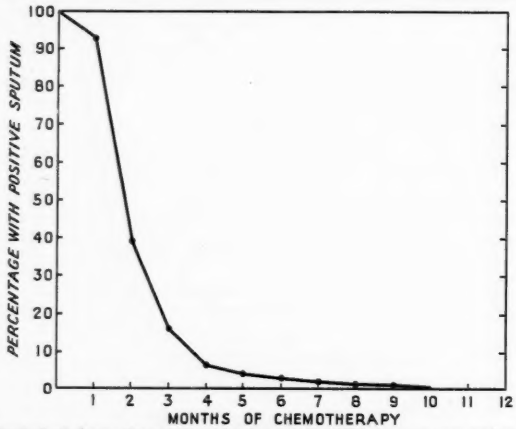
There remain for analysis 530 cases whose bacilli were sensitive to at least two of the three main drugs. The results can be plotted either according to the last date at which a positive bacteriological result was recorded or else the date at which the first of a series of negative bacteriological results was found (table II and figure).

By the end of a month's chemotherapy about 84% of patients have produced their last positive sputum, and by three months only 16% of patients have not yet had their first negative result. By six months only 2·3% have not undergone complete sputum conversion, although it requires a further four months before all cases have become completely sputum negative.

Of these 530 cases, 63 finally had surgical treatment for a variety of reasons. All cases had achieved sputum-conversion by means of chemotherapy *before* the surgery was undertaken. In 2 cases who had wedge resections reversion to a positive sputum occurred after operation; conversion to negative occurred in each case with continued chemotherapy. Thus, sputum conversion was achieved

TABLE II—SPUTUM CONVERSION WITH CHEMOTHERAPY

—	Number positive as judged by date of last positive specimens	Number positive as judged by date of first of series of negative specimens
Number of cases	530 (*100%*)	530 (*100%*)
On admission to hospital	509 (*96%*)	530 (*100%*)
At end of 1 month's chemotherapy	87 (*16·4%*)	492 (*93%*)
2 months' ,,	46 (*8·7%*)	206 (*39%*)
3 ,, ,,	19 (*3·6%*)	85 (*16%*)
4 ,, ,,	9 (*1·7%*)	35 (*6·6%*)
5 ,, ,,	6 (*1·1%*)	20 (*3·8%*)
6 ,, ,,	5 (*0·9%*)	12 (*2·3%*)
7 ,, ,,	3 (*0·6%*)	8 (*1·5%*)
8 ,, ,,	1 (*0·2%*)	4 (*0·7%*)
9 ,, ,,	0 (*0%*)	2 (*0·4%*)
10 ,, ,,	..	0 (*0%*)



Period of chemotherapy required to attain 100% sputum conversion.

in 100% of newly diagnosed drug sensitive cases of pulmonary tuberculosis by chemotherapy alone.

Discussion

Fox and his colleagues (1957) investigating primary drug-resistance between June, 1955 and March, 1956 found 4·1–6·5% in Great Britain as a whole and 2·5% in the area of the Birmingham Regional Hospital Board. Using a different definition of resistance this survey has shown a prevalence of primary drug-resistance of 3% in those cases admitted to the Birmingham chest hospitals.

Whereas Crofton (1958, 1959) thinks that it is possible to achieve 100% sputum conversion in newly diagnosed cooperative patients excreting bacilli sensitive to at least two of the three main drugs, this is not the universal view.

In the report of the United States Public Health Service tuberculosis therapy trial (1959) the comment is made that with each chemotherapeutic combination used in its clinical trials, patients have exhibited a typical bacteriological response to treatment. The response to their regimes is prompt in the early weeks, and at each successive period fewer patients excrete tubercle bacilli until virtually no further change occurs after twenty-four weeks; the curve showing the percentage of sputum conversion to each of the regimes has two common features—a rapid initial response and a plateau with no further conversions by at least six months. This opinion is supported by the results recorded in their paper. In the best previous regimes employed—daily P.A.S. and isoniazid—8·4% of patients able to tolerate this regime still excreted tubercle bacilli at 32 weeks; of those unable to tolerate it, 29% were still positive, making an overall total of 9·8% positive. With a suggested improved regime, in which streptomycin is given daily with daily pyrazinamide for sixteen weeks followed by daily P.A.S. and isoniazid for a further sixteen weeks, the figures for positivity after thirty-two weeks treatment are calculated to be 5%, 2·5%, and 4·5% respectively. Thus the highest sputum conversion achieved was 95·5%.

The Tuberculosis Chemotherapy Centre in Madras (1959) used a combined cachet of P.A.S. and isioniazid. The results were roughly the same for both inpatients and outpatients. For those in hospital the percentage of cases remaining sputum positive using single collected monthly specimens at 3, 6, 9, and 12 months was 26%, 4%, 6%, and 10% for males and 14%, 0%, 0%, and 0% for females, the combined totals giving percentage figures at these periods of 21%, 4%, 4%, and 6·5%.

Our analysis agrees with that reported by Crofton and supports his conclusion that it is possible to achieve 100% sputum conversion in a heterogeneous collection of cooperative patients by the proper use of the three main anti-tuberculous drugs. We consider it important to give daily all the three main drugs until the results of the sensitivity tests are known, when chemotherapy can be adjusted in accordance with the recommendations of the Medical Research Council (1952, 1955).

In performing resistance testing the use of minimal inhibitory concentrations—as used here—is not so reliable as using a criterion based on resistance ratios. The only certain proof of the reliability of the resistance testing is by the results. This survey suggests it is possible to get valuable clinical reports using a criterion based on minimal inhibitory concentrations.

Summary

In all of 530 patients with newly diagnosed pulmonary tuberculosis, whose sputum contained bacilli sensitive to at least two of the three main antituberculous drugs and who were treated in hospital, sputum conversion was achieved by chemotherapy alone.

We gratefully acknowledge the help we have received in compiling this paper from our medical colleagues, Dr. R. J. Austin, Dr. L. F. Dale, Dr. T. B. D'Costa, Dr. Michael Hemming, Dr. Edward Shieff, and Dr. D. C. Waddy, and from Mr. J. L. Clancy who has performed the resistance testing. We would also like to record the valuable secretarial assistance we have received from Mrs. D. Bailey, Miss E. A. Dingley, Miss S. B. Eldershaw, and Miss J. B. James.

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Bread and Flour

A report by the Food Standards Committee [1] makes recommendations for control over the composition, description and labelling, and advertising of bread and flour. The report takes account of evidence received from the food industry and other interests including those concerned with the enforcement of food and drugs legislation.

The main recommendations regarding bread are that there should be a statutory permitted list of the ingredients which may be used in bread; that descriptions of " protein " breads should be controlled; that slimming claims in connection with bread should be controlled; and that exaggerated claims for enrichment of bread or for energy-producing qualities should be prohibited.

The committee suggests that the present regulations which required all flour to contain specified amounts of vitamin B_1, nicotinic acid, and iron, and the addition of chalk (creta præparata) to all flour except wholemeal flour, should be continued for the present and that no change in the prescribed levels of nutrients and chalk is required; that the sampling of flour to ensure that it complies with these regulations should be confined to mills and docks; and that only certain bleaching and improving agents should be allowed for the treatment of flour.

Before deciding whether and to what extent the recommendations should be implemented, Ministers will consider representations by interests concerned. Such representations, from any part of the United Kingdom, should reach the Assistant Secretary, Food Standards Division, Ministry of Agriculture, Fisheries, and Food, Great Westminster House, Horseferry Road, London, S.W.1, by Feb. 17.

1. Food Standards Committee: Report on Bread and Flour. H.M. Stationery Office. 4s. 6d.

Special Articles

EYE SIGNS IN GRAVES' DISEASE

THE eye signs which accompany Graves' disease are so characteristic of the condition that it would be a great convenience if there was some form of standardised nomenclature with which to describe them. Eponyms like Stellwag, von Graefe, and a host of others only add confusion and are often used to describe signs which their originators never intended. The occasion of the Fourth International Goitre Conference, held in London in July, provided a unique opportunity for a group of people interested in eye signs to sit round a table and try to reach some agreement on classification.

Sir Russell Brain took the chair, and the following were present:

Dr. Brown M. Dobyns (Cleveland, Ohio), Prof. Russell Fraser (London), Mr. Keith Lyle (London), Prof. James Howard Means (Boston), Dr. Rulon W. Rawson (New York), Mr. Selwyn Taylor (London), and Dr. Sidney C. Werner (New York). Dr. Nigel Oakley (London) acted as recorder.

EXOPHTHALMOS, PROPTOSIS, OR EYE SIGNS

The word exophthalmos stems from the Greek and implies that the eye is out. Proptosis is also Greek in origin and means that the eye is pulled forwards. Ophthalmic surgeons have in the past used the word exophthalmos to imply an active protrusion and proptosis a passive one; the latter being due to an increase in the retrobulbar mass. This is not a satisfactory distinction, nor is there a scientific basis for it.

Exophthalmos (measured in millimetres of protrusion) appears to be the most satisfactory term which can be used to describe the disorder of the orbital contents in Graves' disease; but other changes, such as lid retraction, are not necessarily implied by it. Exophthalmos is not, therefore, considered a completely satisfactory descriptive term. It was agreed that the term " protrusio bulbæ " was superfluous.

The possible alternative to using the above terms would be to refer to this phenomenon as " eye signs of Graves' disease ". It must, however, be recognised that eye signs similar to those seen in Graves' disease may be seen in patients with Cushing's syndrome or even in patients with kidney disease, and one member made a strong plea for the term " endocrine ophthalmopathy ". However, since the whole clinical picture may not be a single physiological entity, it seems best to adopt a purely descriptive nomenclature.

PROGRESSIVE CHANGES

On turning to the natural history of exophthalmos it was considered that one of the important reasons for trying to document eye signs accurately was to predict future changes, even though this might be very difficult. There was fairly general agreement on a number of specific points, among which were the following:

Loss of visual acuity in Graves' disease rarely occurs without some degree of exophthalmos and never without increased retrobulbar pressure. This loss falls into two separate categories: (*a*) due to corneal ulceration and resulting corneal opacity; and (*b*) due to defects in the visual fields including paracentral or central scotomata, and these are due to pressure on the optic nerve or, possibly, circulatory disturbances.

True lid-lag is virtually specific to hyperthyroidism and usually disappears on return to a euthyroid condition. It may be due to increased tension in the levator palpebræ superioris.

Even the most severe orbital lesions may show complete regression.

Permanent impairment of function in the orbital contents is usually related to the duration and severity of the changes.

CLASSIFICATION

When it comes to the classification of eye signs there were almost as many different classifications as there were people present. However, there was general agreement that " malignant exophthalmos " (though a misleading term) referred to those cases in which protrusion continued to progress so that visual acuity was impaired and corneal ulceration or even loss of the eye appeared likely. It was pointed out that lid retraction may, in some instances, be due to increased tension in the levator palpebræ superioris rather than to contraction of the unstriped muscle in the upper eyelid. Such a mechanism should be carefully distinguished from the mechanical effect of mere protrusion of the eyeball on the upper lid.

RECORDING OF EYE SIGNS

There was general agreement that eye signs should be carefully recorded and measured as far as possible; and one list, which most members took least objection to, had eight items as follows:

1. Eyeball protrusion—measured from the lateral rim of the bony orbit.
2. Lid retraction—measured at rest from the upper iris margin with the eyes looking horizontally forward.
3. Lid-lag.
4. Bulge of upper lid.
5. Bulge of lower lid.
6. Chemosis and peripheral conjunctival congestion—grades 1–4.
7. Decreased resiliency of the eyeball estimated by pressure upon the closed eyelids.
8. Impairment of ocular movements.

When the abnormality cannot be directly measured it is useful to define different grades of severity, and a simple way of so doing is to give a number of plus signs, from + to ++++. It is then desirable that the same doctor always makes the assessment. Better than this is to measure, where possible, as in 1 and 8.

For eyeball protrusion different workers attach importance to a variety of methods. The Hertel exophthalmometer was considered by most to be a valuable aid in measuring the degree of protrusion, but again it was stressed that the same observer must use the identical instrument when measuring progress in any one patient. Accurate lateral photographs were also considered of value in assessing progress; and reference was made to an apparatus which fitted over the head and carried a mirror at the angle of the orbit together with a millimetre scale so that the eyes could be photographed showing the degree of protrusion and thus provide a permanent record. The Copper orbitonometer was generally regarded as a most useful research tool, but is not suitable for general clinical application. It does not appear to have yielded important information.

CONCLUSION

Since we remain ignorant of the ætiology of Graves' disease it is not surprising that general agreement on nomenclature was not reached. Some preferred the " eye signs of Graves' disease "; others were unwilling to drop " exophthalmos " while appreciating its limitations; one member preferred " endocrine ophthalmopathy ". However, all agreed that the careful recording and grading of the eye changes, as described above, was of real value.

SELWYN TAYLOR.

The Widdicombe File

LXVII.—ON BEING AN OMP

DEAR GURNEY,

I didn't get a chance to make my point properly the other night. But, as you seemed openminded about Omps, I'm writing it down. If it's true, as you said, that there's a shortage of ophthalmic consultants in the N.H.S., it could be important.

Quite a lot of people, adequately qualified in ophthalmic medicine and surgery, earn the greater part of their living by carrying out refractions through the Supplementary Ophthalmic Services; and many of these Ophthalmic Medical Practitioners (O.M.P.S) are also attached in some capacity to a hospital where they can do clinical work and surgery. But some have no such hospital connection, and spend all their working days on the refraction of the eye—which (if they work hard enough) can in fact bring in quite a considerable income.

Such a person to my way of thinking is properly designated an Omp. Not for him the glamour of the keratoplasty, the doubts and sorrows of toiling, year in and year out, with a chronic uveitis, the rewarding glow attending the restoration of sight to someone in danger of losing it. His placid life is ruffled by a minimum of responsibility, his success dependent upon an ability to carry out accurately the same procedures over and over again. It is rather as though a lawyer, meticulously and completely qualified, elects or is condemned to spend his entire existence in the occupation of drawing up wills.

But the Omp may have drifted into his vegetative existence faute-de-mieux rather than by design; and not so very long ago the Ophthalmic Group Committee said that all Omps should be encouraged to undertake some kind of work in the Hospital Eye Service. The question is whether such work is available.

To qualify for his " title ", an Omp needs to undergo a considerable training, and has to have both academic and practical experience in ophthalmology. Indeed the qualifications of some Omps are at least equal to those of some of their more fortunate brothers who are classified as " consultants ". It seems a pity therefore that their activities should be so severely circumscribed and restricted. For they are permitted by law to carry out no form of treatment.

Herein lies, to my way of thinking, a serious imperfection in the present scheme of things. A patient attends a Medical Eye Centre, where an Omp does his work for the most part, because there he may be examined by a Medical Eye Specialist. He often has, in addition to a possible refractive error, some comparatively trifling ophthalmic complaint, such as blepharitis, for which he wants advice. He is, to say the least, puzzled when the specialist says in effect " you have a minor affection of your eyes which is easily amenable to treatment, but I am not permitted by law to advise you what to do about it—you must see your general practitioner about this, and he'll refer you to the hospital if he thinks it is necessary ".

The patient's reaction to this may well be " What's the use of my attending a Medical Eye Centre at some distance from my home to see a Medical Eye Specialist if he can do no more than refer me to my G.P. to whom I could have gone in the first place ? I could just as well have gone to the sight-testing optician whose shop is just around the corner ". And so the whole concept of the Medical Eye Centre, which is to encourage the public to have their eyes examined by an ophthalmic surgeon, falls flat on its face. Of course I know the considerations which lie behind the strict limitation of the activities of the Omp; but the patient doesn't know about them; and his irritation at not getting the help he expects from the Medical Eye Specialist doesn't encourage him in future to have his eyes examined by such a person. Which is a pity.

On the other hand one reads and hears a good deal about overworked hospital outpatient departments, and in some cases delay in making appointments. Here surely is a siding into which some of the routine and time-consuming work of the ophthalmic outpatients could reasonably be shunted ?

Take the case of the patient requiring periodic perimetry. Such a case, diagnosed and properly referred by the Omp to the Hospital Eye Service, is not seen again by him certainly until a further refraction is indicated; and, if the refraction is later done at the hospital, perhaps never again. This deprives the Omp of any further interest in the case. But, the patient having been referred in the first place and the diagnosis confirmed, it would surely not be very difficult for him to be referred back to the Omp for routine perimetry and further observation ? He can always be sent back to the hospital when the signs indicate this. Yes, one knows that at present an Omp may not normally re-examine a case in less than a year, and one can hear the horrid word " abuse " rumbling off-stage; but if a consultant, in referring a case back to an Omp for perimetry, specifically states " this case requires examination every three months ", is this not a fair safeguard ? And it should not be impossible for ingenuity to cover other instances. The additional cost involved, set against the Ben Nevis of Supplementary Ophthalmic Services expenses or the Everest of the N.H.S. budget, would perhaps take on the dimensions of a sizable molehill—remembering that new glasses would not normally materialise from such " repeat visits ".

As things are, I gather there's some doubt whether an Omp, seeing a patient suffering from, say, blepharitis, is entitled to give him a prescription for an appropriate remedy to be dispensed at his own expense; or even whether, strictly speaking, he is entitled to suggest to a general practitioner a course of action which would be likely to benefit a patient suffering from a complaint which could reasonably be treated by him. Now that I am Omp 72 (retd.) I hope I shan't get into a great deal of trouble if I confess to having transgressed in both respects with some frequency. I feel that some patients were not ungrateful, and I can't believe much harm was done. Whether the G.P.S concerned approved is not for me to say. At least I had no complaints.

In my opinion, therefore, the ability and potential of the Omp is not at present being utilised to the full, and the pressure on hospital outpatients could well be reduced by a redistribution of certain kinds of routine work. There seems to be a sad tendency these days for people to say in shocked voice " Oh, but you can't do that; it isn't provided for in the Act ". This has always made me feel that if the Act is demonstrably susceptible of improvement, then it is high time someone amended it. I know of no other branch of Medicine in which a practitioner is for all practical purposes debarred from clinical work; and though the fruit at the top of the ophthalmological tree may still be as sweet as in former years, fewer students of moderate ability are likely to look for a place on the branches nearer the ground. And to those who see in this

an automatic selective mechanism, I would say that ophthalmology cannot thrive on selected material only: for one thing there will not be enough of it, and for another in *all* branches of medicine useful work, and this includes clinical work, is done by the humbler members. Such as

Yours sincerely,
O. D. LEA.

Parliament

Penology in the Affluent Society

INTRODUCING the Criminal Justice Bill [1] in the House of Commons on Nov. 17, Mr. R. A. BUTLER, the Home Secretary, admitted that he did so against a rather sombre background. Last year, roughly a third of those convicted for indictable offences were between the ages of 14 and 21 and the total number of such offences known to the police was more than double that of 1958. No one method or one type of punishment would suffice to solve the problem of crime, but in his view some essentials must be tackled at once. We must ensure that the police were brought up to strength and that their relations with the public were good. We must expand the probation service to meet the increasing demands imposed by the high level of crime and the increasing responsibilities to be imposed by this new Bill. We must remember the needs of the prison service. He had appointed two bodies to examine the law. The Criminal Law Revision Committee had already submitted a report on the law relating to suicide and attempted suicide, and were now considering larceny. The Streatfeild Committee were considering the machinery of the superior courts. Lord Ingleby's Committee had surveyed our system of juvenile courts and some of their recommendations had been fitted into the present Bill. Others, notably the proposal to raise the age of criminal responsibility, needed further consideration.

A method of punishment which we have discarded is corporal punishment, and Mr. Butler said that the Advisory Council on the Treatment of Offenders' report [2] confirmed the Government's judgment that it should not be reintroduced. He accepted the Council's view that the present powers of the courts for serious offences was adequate. What was not adequate was the power to fine for less grave offences, and some proposals to this end, in respect of juveniles and their parents, were included in this Bill. He added that he hoped soon to receive the report of the working party which was considering a scheme for compensating victims of crimes of violence.

He recognised that the Bill would depend on the right buildings being available and the Prison Commission was driving ahead with the largest programme of building and refurbishing prisons that we have known for many generations. 3 new open prisons had already been completed, 3 detention centres would be open in the next three months. By the latter part of the year he hoped to have 10 detention centres in being, giving a total of 12. They were also planning to spend in the next few years about £5 million in the modernisation of the premises of approved schools. It was intended to set up a small number of closed units, attached to existing schools, to provide for observation and treatment as well as secure custody. Improved premises would be of limited value unless enough staff of the right calibre were attracted to the service and he had been struck by the difficulties arising from the general shortage of qualified social workers. With the help of the Central Training Council in Child Care they were extending the training facilities for the staff of approved schools. Improved salary scales had lately been agreed and they were seeking to improve the living conditions of residential staff.

Reviewing the clauses of the Bill, Mr. Butler described the provision for aftercare as one of its "most important and potentially beneficial proposals". Nothing we could do for a young man while he was in prison was of any value unless we could negotiate the readjustment to freedom successfully. Extension of compulsory aftercare would create new problems of organisation and he was going to ask the Advisory Council to review existing practice. The proposal in the Bill to amalgamate the Prison Commission and the Home Office was made because the original division of responsibility between the Commission as an executive authority and the Home Office as the policy-making body had disappeared. It did not foreshadow any drastic change and it would not mean the dissolution of the Prison Board as a team of administrative and professional officials. By this integration it might be possible to draw closer the prison and probation services and the approved school and borstal services. Eventually he would like to see what was now the Prison Commission becoming part of a wider organisation covering all Home Office responsibilities for criminal justice and the treatment of offenders.

Mr. GORDON WALKER thought that the Bill made a little progress in the right direction but was inadequate to the tasks and crises facing the country. Our research was still lamentably inadequate and our criminal statistics wholly misleading in many respects. Sir KENNETH PICKTHORN did not accept the assumption that trying to reform was superior to trying to deter. It was no good the Home Office getting more and more progressive if the result was an increase in crime. The moral improvement of the criminal should be an indirect object. The object of imprisonment should be the prevention of crime.

Sir THOMAS MOORE found the Bill admirable, but suggested that it had a strange kinship with the 1948 Act with its insistence on more detention centres, more remand homes, and more and better prisons. These, however, had not materialised, often with tragic results. He knew of a boy of 16½ sent for two months to a prison for hardened criminals because there was no room in a borstal. He was tempted to say that a good whipping would have done the bou less harm. He was disappointed in the Advisory Council's report on corporal punishment. He thought that the Council had relied too greatly on the Cadogan report of 1938. Since then the social and economic conditions of the country had improved. Yet we had a gross and dramatic increase in deliquency and crimes of violence. He asked the Home Secretary to consider giving the courts, for a trial period of five to ten years, the right to use the cane for criminals up to 17 years of age, and the birch for criminals of more than 17. The cat, with its implication of sadism, should be dropped, and he reminded the House that only the Home Office retained this form of punishment in its own prisons.

Mr. CLEMENT DAVIES pointed out that the Ingleby Committee had considered the problem in the early stages, not after the crime was committed, but when the child's mind might have been influenced. In our primary schools he would like to see more attention paid by doctors to the mind rather than to body health. If we gave more care to problem children in schools, he was sure there would be less delinquency.

Mr. CHRISTOPHER MAYHEW was one of the many speakers, who, unlike Sir Thomas Moore, accepted the Advisory Council conclusions. Their report in Mr. Mayhew's view had conclusively shown that corporal punishment made no difference one way or the other to the future career of a person who was punished. This linked with the important point raised earlier in the debate by Sir GEORGE BENSON, that whether an offender went to a borstal, prison, or a detention centre the evidence suggested that it had no effect on his career. Whether an offender would go straight or not could be predicted with great accuracy from his family background, character, and previous career before he was sentenced. If we accepted this disheartening conclusion, Mr. MAYHEW suggested that the best penal system would be one which filtered out from the rest those who would go straight anyway. They should be released as quickly as possible, and the others shut up, humanely and productively, for a long time. Turning to the offender's social background, he said that our affluent society might have been designed to aggravate and exploit any weakness of personality.

1. See *Lancet*, Nov. 12, 1960, p. 1082.
2. See *ibid.* Nov. 19, 1960, p. 1149.

It stressed ambition, success, and wealth. It brought strong pressure on young people, through advertising and salesmanship, to spend freely on cigarettes, clothes, drinks, and all the rest of it. It repeatedly offered something for nothing as in premium bonds or pools. Our newspapers, films, and television too often glamorised crime for our amusement and entertainment. It had been said that "a society gets the crime it deserves". He believed that was true of our overcommercialised affluent society.

Mr. W. F. DEEDES pointed out that the detention centres of the future would have enlarged functions, and he thought that the administrative consequences were being taken a little lightly. The existing centres were staffed by volunteers from the prison service. Would it be possible to get volunteers for the ten new centres? The centres would be receiving an increasingly mixed bag of offenders. We must recognise that among juvenile delinquents today there was a hard core of thoroughly vicious, amoral, dangerous youngsters. If the detention centre was to be the civilised alternative to the birch, it must be not simply an instrument for the reclamation of misguided youth. It must also be the principal means of protecting society against violence which was often rendered more beastly, thoughtless, and dangerous by the immaturity of the attacker. Mr. T. L. IREMONGER had found quite a few psychopaths in approved schools and borstals. He suggested that those should be weeded out and given separate treatment for the sake of the staff and the rest of the school. The Mental Health Act might be used to detain them for treatment.

Sir REGINALD MANNINGHAM-BULLER, the Attorney-General, in summing up the debate, said that one of the main reasons why he had supported the retention of the birch in 1948 was to avoid sending young offenders to prison. When this Bill came into effect it would mean that young offenders would not ordinarily be sent to prison and the main argument for judicial corporal punishment would fall to the ground. The rate of crime in 1959 among males in the age-group 15 to 17 was almost twice the 1954 figure, and he could not have supported this Bill unless he was satisfied that it was in no sense a soft Bill. In fact it provided a more strenuous and rigorous regime for young offenders than they would have to undergo in a local prison. It was against this background that any proposals for the reintroduction of corporal punishment must be considered and he did not think that it would be right or wise to treat lightly the conclusion which the Advisory Council had reached unanimously after hearing a mass of evidence from people of varying views.

Parliamentary Medical Committee

The following have been elected as officers of this all-party committee: Sir Malcolm Stoddart-Scott (chairman), Dr. J. Dickson Mabon (hon. secretary), and Dr. Donald Johnson (hon. treasurer).

QUESTION TIME

Diesel Fumes

Mr. N. N. DODDS asked the Minister of Health, as representing the Minister of Science, if he would give details of the experiments carried out on behalf of his department which show that diesel fumes are not endangering health.—Mr. ENOCH POWELL replied: Investigations into the effects on health of diesel exhaust fumes form part of the programme of research on air pollution undertaken by the Medical Research Council. They have included statistical studies on a large group of patients with lung cancer, which showed that in this group there was no greater proportion of persons who might have been expected from the nature of their employment to have greater exposure to vehicle exhaust fumes; and a study on London Transport employees, in collaboration with the chief medical officer of London Transport, which provided no evidence of significantly greater mortality from lung cancer among men working in diesel-bus garages. Analyses of the air in bus garages and busy streets have shown that motor exhaust fumes are only one of many pollutants and that their content of benzpyrene, a known cancer-producing agent, is very small in relation to the total amount in the atmosphere from all sources. Even in congested spaces, such as vehicular tunnels, pollution from exhaust fumes has been found to be no greater than the pollution of an urban atmosphere by coal smoke on many winter evenings. It seems reasonable, therefore, to deduce from these findings that diesel fumes are not endangering health.

Manufacturing Expenses

Mr. KENNETH ROBINSON asked the Minister of Health whether he was aware that drug manufacturers included in their manufacturing expenses such promotion expenses as continental holidays offered as prizes to pharmacists; and to what extent he took into account such expenses in approving the costs of new drugs prescribed within the National Health Service.—Mr. POWELL replied: I am aware of one recent instance of this, but am told that the firm concerned does not intend to use this type of sales promotion in future. The costs of new drugs prescribed within the National Health Service are not subject to my approval. Mr. ROBINSON: Does not the Minister agree that this type of advertising, which was indulged in by Aspro-Nicholas in trying to introduce a new antibiotic, can only reflect adversely on the pharmaceutical industry as a whole? Will he do everything in his power, by persuasion, to see that it does not happen again?—Mr. POWELL: Yes.

Group Practice Loans

Mr. L. A. PAVITT asked the Minister why the average time for approving loans to group practices was $4^1/_2$ months; and if he would take steps to shorten this period.—Mr. POWELL: The committee needs this time to study the proposed arrangements and plans, to visit the groups, and to get agreement to any modifications necessary.

Mr. PAVITT asked the Minister what was the maximum loan granted per doctor in a group practice receiving loans from the fund established for that purpose.—Mr. POWELL: £2500.

Drugs and Dressings for Private Patients

On a rough estimate, the extra annual cost of providing drugs and dressings on National Health Service terms for residents in Britain not now registered with an N.H.S. doctor might be between £2 million and £3 million.

Hospital Development Unit

This Ministry of Health unit comprises 13 full-time and 8 part-time professional officers. The function of the unit is to ensure that the most up-to-date knowledge and experience is assembled and brought to bear on all aspects of hospital building. It has published a bulletin on operating-theatre suites and is preparing for publication further bulletins on specific departments, in addition to some 30 building notes on the features and standards which should be embodied in the design of modern hospitals. It will itself be responsible for an outpatient department and kitchen which are to be built as development projects.

Medicine and the Law

Anæmia Due to Potassium Perchlorate?

AT a Southend inquest on Nov. 15, an open verdict was returned on a 29-year-old woman who died after treatment of a thyroid condition with potassium perchlorate.[1]

A senior medical registrar said in evidence that treatment with this drug had been begun in June. The thyroid symptoms were relieved, but by Sept. 29 the patient was extremely anæmic. "There is no previous record of this drug producing the failure. There have been reports where white blood cells have not been produced as a result of the drug but these patients all recovered."

1. *Times*, Nov. 16, 1960.

In England Now

A Running Commentary by Peripatetic Correspondents

THERE was a time (it seems odd to think of it now) when we knew very little about libraries. We began our official career as a custodian of books some years ago, as a member of the Preclinical Library Committee, recommending books in a carefree way and adopting a proprietorial air over the journal racks when we visited our domain. By diligent attention to detail we rapidly climbed the ladder of promotion to the post of Chairman, and in counsel with our studious and reliable Preclinical Librarian we developed such striking lines of policy as the provision of red linoleum for the floor and the planting of flame-trees outside the windows to keep the sun off. We even asked the university for an air-conditioning unit so that the students might read without the risk of heat exhaustion. Naturally, subversive notions of this kind could not be tolerated in any respectable university, and we awoke one morning to find that we had been kicked upstairs into membership of the University Library Committee itself. This body operates on an altogether more rarefied plane, meeting in the Vice-Chancellor's room and fortifying itself with tea and chocolate biscuits.

After our translation we made a general tour of the University Library to examine the ramifications of our new responsibility. We prowled at will through the forbidden hinterland, entering the reference staff-room, the cataloguing staff-room, the orders room, and the acquisitions department. We visited the bindery, the photographic room, and the book-lift. A chat on logistics with our learned and genial Librarian revealed to us that each undergraduate reader required 25 sq. ft. of space, and each postgraduate 35 sq. ft., that the accepted ratio of seats to full-time students is 1 : 3, and that the standard height of book stacks is 7 ft. 6 in. The whole atmosphere was quiet and scholarly, far removed from that of our early struggles in the Preclinical Library.

Finally we visited the reading-rooms. The books did not frighten us so much—after all, we had been nipping in and out to borrow Trollope for years, and it had not escaped our notice that there were other sorts of books around—it was the journals which pointed up our narrow-minded professional outlook. In agriculture, for example, it seems that they read *Beef Situation* and *Herbage Abstracts*. The chemists receive, among others, the *Perfumery and Essential Oil Record*, and *Pipe Roll Society* is required reading for lawyers. In education they spend happy hours reading *Let's Dance*, or, more soberly, *Laban Art of Movement*, and, for a dreamy mood, the enigmatic *Etude*. The zoologists are addicted to *Insects Sociaux* and *Tuatara*, and the psychologists find instruction as well as relaxation in studying the *Journal of Projective Technique*. The engineers—solid earthy creatures—while away their long weekends with *Beama, Diesel Engine Users' Association*, and *Muck Shifter*.

At the next meeting of the Library Committee I am going to suggest that some of these journals should be routed through the Preclinical Library to broaden, for the medical student, the straitened educational experience which we all so much deplore. It is safe to say that no-one could read *Muck Shifter* and remain unbroadened, and a study of *Beef Situation* could only expand the restricted technical horizon. In return we could offer the Faculty of Arts a choice of *Brain* or *Gut*, and the Faculty of Education might like to glance through a few recent issues of *Blood*.

* * *

One of my quirks is to write down, in a big exercise book, what I think of each book I read. I have just been looking back at what I recorded twenty years ago about *Lady Chatterley's Lover* when I read it at the age of twenty-five:

"I think it's a good book—not by any means pornography. I think it's a good story and I think the 'message' of the coming downfall of industrial civilisation unless we have more 'tenderness' is a very feasible idea. But I don't like the coldness of it—it's very hard and bare—there's no happiness in the book: but there was no happiness in Lawrence's heart when he wrote it. I liked it better than *Sons and Lovers*, but they share this barren chilliness that's so dispiriting. Strangely enough, both books are also at times highly romantic, and the descriptions of the countryside and the flora and fauna are almost lyrical. He was a queer mixture: more of a poet than anything else, in the sense of temperament. There are one or two surprising bits of good characterization and action-story-telling in this book: as, for instance, the time that Clifford's chair wouldn't go up the hill."

I had forgotten all about the incident of Clifford's chair, but I suppose the remarkable thing about these comments is that they include no mention of four-letter words. It looks as though their presence made no great impact upon me.

* * *

My happiest memories of that pharmaceutical feast, the London Medical Exhibition, go back to 1946. As a first-year preclinical student I had borrowed my father's invitation. It lent me a spurious eminence and opened every door, and I even ended up with a free tea. Still, even this year, over the second stall of this decorous and decorated market-place I met my tennis partner of ten years ago; and we had exactly the right amount of time to catch up with our news. Round the corner behind a cardiograph or something, the size of a house, meandered my first medical superintendent—long since abolished poor man. At this point it struck me that the exhibition should stimulate the reunion aspect. Perhaps the prospectus could allot days and times so that the old boys of St. Cecil's, say, would know there was the most chance of seeing old pals at 3.30 on Tuesday.

* * *

The undertaker's clerk and I met over a cremation form. The new crematorium, it appeared, had been open for over two months. "Oh yes, it's doing very well, I believe—and fancy *you* not knowing it was open all this time, doctor."

* * *

A difficult problem in human rights was raised last year by a call from the local vet, whose practice covers one of the remoter valleys of our western fringe; a valley where Government had early insisted that all cattle should be healthy. Within the last few months, he declared, 14 fine Friesians had become violently tuberculin-positive, and had therefore gone the way of all flesh at great expense to the taxpayer; did I know anything, he asked, about Farmer Cobbleigh, who looked very unwell, and would I please take any necessary steps?

This local notable's records showed that he had indeed been treated some years before with antibacterial agents for a large pleural effusion, but had absconded and stoutly refused our further attentions. Ignobly, I asked the health visitor to call on him, but she found the portcullis firmly down. His family doctor went into the assault next, but was met with abuse and showers of stones (well aimed from the spinning gallery). Finally, the senior partner from the next valley donned a tin hat, and took the place by storm in his Landrover, after which he carried Cobbleigh in triumph directly to the hospital. His chest radiograph showed galloping consumption of such exuberant quality that no normal lung was to be seen. Now, after a year in hospital, he is no longer infectious, and less breathless and more robust than most people; and he has perhaps wisely obtained work as a clerk.

There was no further epidemiological problem, for he had no human contacts at all; in fact he had done all the milking himself for years for this very reason.

* * *

I have had a scooter, of one kind or another, for some years, but until lately I did not feel it belonged with my colleagues' motor-cars. I used to park it a little way from the main entrance, and I always removed my crash helmet before I went inside the hospital. But now at last, the scooter has been accepted as a means of transport for the medical profession. In the paper the other day I read the headline "Drugs Stolen from Doctor's Scooter".

* * *

In a transatlantic journal I came across a report on "Salmonellosis spread by a dietary supplement of Avian Source". Pâté de foie gras was my first guess; or could it be larks' tongues? No—egg nog.

Letters to the Editor

TUMOURS OF THE BLADDER

SIR,—In your leading article of Nov. 12 you make the comment: " In the past decade the causes, treatment, and prevention of bladder tumours have aroused much interest. Fascinating questions surround the incidence of this disease. Why is it increasing in younger males? Why is it apparently commoner in towns than in the country? Why is it rare in Japan and India? Now that β-naphthylamine is no longer employed in the dye, chemical, or rubber industry, which industries still use carcinogens such as benzidine?"

In my opinion it is high time indeed that honest, unequivocal, and comprehensive answers were openly given to questions like the last. In fact, for reasons set out below, the question does not go far enough. It should be extended to cover all the recognised bladder carcinogens and should relate to past as well as present usage.

Part of the mortality from tumours of the bladder in this country is unquestionably due to occupational factors. The results of using the chemical agents so far known to be carcinogenic have taken a long time to become manifest. Some of the substances concerned are no longer in common industrial use, and others are used with much more protection of workers than in the past, but the effects, already determined before these changes took place, will continue to show for years yet to come.

It follows that an epidemiologist is precluded from answering a vital question, posed below, unless he has a knowledge of what known carcinogens have been used, in what processes they were employed, in what parts of the country these processes were carried out, and between what dates they were operated.

The vital question facing the epidemiologist is this:

Taking into account our knowledge of the epidemiology of bladder cancer resulting from exposure to known carcinogens in the dyestuff manufacturing industry [1] and our much less detailed knowledge of bladder cancer resulting from exposure to certain antioxidants in the rubber manufacturing industry,[2] can we say that the present mortality pattern from bladder cancer within the country is compatible with the hypothesis that all the major industrial bladder carcinogens have been identified and the hazards resulting from them acceptably mitigated?

Side by side with this problem of social medicine is the medical practitioner's concern with the individual patient and his dependants. A statutory instrument [3] prescribes for benefit under the National Insurance Act tumours of the urinary bladder which occur in workers in insurable occupations who have been, in the course of their work, exposed to certain named substances at any time after July 4, 1948. The industrial processes where this may occur are often such that the worker operating them is unlikely to know the chemical nature of the substances he uses. Many medical practitioners feel it is their duty to give advice as to when a claim under the Act would be justifiable, but they are unable to do so because of the absence of published information about the industrial uses of the substances concerned.

There may be ways whereby members of the public can obtain this information which, to be useful, must be free from the restriction of confidentiality. If so, I have been unable to discover them. In unsuccessful attempts to do so in the past I have drafted questions for a Member of Parliament to lay before the House and have put the same questions to an appropriate official of the Factory Department.

One author seems to have been more successful, for a categorical statement that benzidine has in the past been used in the rubber industry and that its use has now been abandoned has recently been published.[4] Unfortunately no information about how or where the material was used, the date when usage ceased, or the source of the information was given.

May I use the authority of your columns, Sir, to urge that an independent person or body is given the facilities to compile and publish a reliable history of the industrial use of the known bladder carcinogens? Without this information some of the " fascinating questions " you mention can never be answered, and without it medical men cannot give adequate advice to patients who might be entitled to industrial injury benefit.

London, S.W.5. R. A. M. CASE.

MODERN CLINICAL BIOCHEMISTRY

SIR,—Is it not true that the only justification for our professional existence is the benefit to the patient? If we admit this, the studied self-worship of the ultra-specialist and that of the lonely egocentric on the peak of his pyramid of subordinates, alike appear ridiculous. The problem at the centre of this correspondence becomes much simpler: how can we provide patients with the widest range of laboratory care, taking due note of the frequency with which different types of laboratory assistance are needed, the readiness with which the patient can be brought to hospital, and the availability of specialists of various kinds.

In large cities patients can be moved by ambulance quickly and smoothly, and distances are such that few suffer injury by a journey across the city. In cities, therefore, we need few hospitals, but each must be large and carry a staff which includes most specialties. In city hospitals we therefore need specialists in all four branches of laboratory medicine—pathology *sensu Anglicano*, a fourth meaning for Dr. Hendry (Nov. 19)—but they should be ready and able to exchange their views on any matter which may concern the patient directly or indirectly (for example, the bacteriologist, as hygiene officer, may have to forbid the entrance to the wards of a biochemical technician suffering from a boil). It is therefore desirable that departmental heads be on terms of amity rather than enmity, and that each should have some acquaintance with the work of the others, even though this acquaintance be superficial, such as that acquired by a registrar who spends only 6 months in a department.

In many country areas a hospital with 200–300 acute beds may have to serve the needs of a small town and a large and sparsely populated rural district. Such a hospital is necessarily staffed mainly by general physicians and surgeons, and it is unreasonable to provide a full staff of laboratory specialists who would be unable to obtain enough material to foster their especial skills. However, in such centres the patients who need really esoteric investigation are rarely acutely ill, and can usually be transferred to a larger centre. Such hospitals need a general pathologist who knows something about all branches, but more about one or two. My experience is that for every patient who needs a complex series of chemical investigations done within a few hours, ten need blood-transfusion, and a hundred need bacteriological or hæmatological investigation; with rare exceptions histopathological investigations could be carried on some miles away. It seems to me that the pathologist attached to such a hospital needs to be a very well-trained bacteriologist, to know quite a lot about blood-transfusion and hæmatology, and to have some knowledge of clinical

1. Papilloma of the Bladder in the Chemical Industry: a study of its cause and prevention. Association of British Chemical Manufacturers. London, 1953.
2. Case, R. A. M., Hosker, M. E. *Brit. J. prev. soc. Med.* 1954, **8**, 39.
3. S.I. no. 1740, 1953.
4. Poole-Wilson, D. S. *Proc. R. Soc. Med.* 1960, **53**, 813.

chemistry—last because lack of it is likely to kill fewer patients than lack of the other skills.

The function of the pathologist in his hospital will also vary according to the time spent in hospital by consultant clinicians. The diagnostic acumen of Dr. Osborn (Nov. 5) would hardly be required if his clinical colleagues spent most of their working time inside the hospital—and it can hardly be exercised on many of the patients who occupy the 2000-odd beds for which he is reputed to be pathologically responsible without his being absent from his laboratories for most of the working day. If physicians are rarely in the hospital, the pathologist usually takes their place—often willingly—but I doubt whether the substitution is for the good of the patient.

There is no doubt that there are about 200 centres in which a biochemist or chemical pathologist is needed, and which is appointed will depend on various committees' appreciation of local needs. For my part, I believe that the best solution would be to recruit 1st-class or 2nd-class honours graduates in chemistry and pay them a salary while they undertake their medical studies, and complete not only their intern year but also 2 years as registrar in general pathology (*sensu Anglicano*), so that they will have that acquaintance with their colleagues' specialties which will enable them to cooperate fruitfully.

However, there are at least as many centres in which the general pathologist is inevitable, at least for a generation, and I submit that since (1) every medical graduate has learnt some chemistry, (2) pathologists *sensu Anglicano* are highly selected, and (3) embryo pathologists who wish to learn more chemistry are even less common, it seems not to be excluded that the registrars selected for an extra year's work in chemistry may acquire quite a useful knowledge, and might even be stimulated to go on learning.

There is no reason for medically qualified biochemists to avoid the hospital service, for there are consultant posts, and I believe more would appear were the money available slightly increased and the supply of qualified persons larger. But I have great sympathy with the non-medical biochemists in their difficulties outlined by Dr. Woolf (Nov. 12) and confirmed by Mr. Love (Nov. 19). Hospital administrators, medical or lay, seldom realise that the professional future of the non-medical biochemist depends almost entirely on the original work he can undertake, and I am sorry to hear that he still suffers the mixture of suspicion and patronage which I noted 20 years ago among junior medical, nursing, and administrative staff—but which was so strikingly absent from my senior medical colleagues, to whom I still feel a sense of indebtedness and gratitude. I do not know how these problems can be resolved—perhaps by educating our administrators—but I see no advantage in making non-medical biochemists the only advisers on clinical chemistry to the regional boards, when there are doubly-qualified men who are at least as suitable for this duty.

London, N.W.10. GEORGE DISCOMBE.

THE FEMALE PROSTATE

SIR,—Mr. Rhodes (Oct. 15) asks what I meant to convey by approving (Oct. 1) Mr. Moore's statement[1] that "It is unfortunately still traditional for urinary symptoms in the female to lead to a gynæcological consultation . . ." The answer is that in my opinion urinary complaints in female (or male) should be treated by those specially trained in urology, just as patients with gynæcological symptoms should be seen and treated by those trained in gynæcology.

Mr. Rhodes further says: "the relationships between gynæcologists and urologists are such that they each need the other at times". I agree entirely, but why limit these relationships to the two specialties only? Surely this applies to all of them.

1. *Lancet*, 1960, i, 1305.

As to backbiting, &c., would a proctologist be high-horse-riding if *he* and not a gynæcologist saw and treated postpartum hæmorrhoids? It is to be hoped that Mr. Rhodes's choice of words ("backbiting and high horse") is merely his personal manifestation of the truth of the old Talmudic saying: "Rivalry of Authors enriches Wisdom" (*Baba Bathra*, **21**, p. 1).

Tel Aviv. HERZL KOOK.

THE BORDERLINE FOR SEVERE SUBNORMALITY

SIR,—As Dr. MacMahon and Dr. Clarke (Oct. 29) pointed out, it will be unfortunate if, at a time when great changes are taking place in the mental-deficiency services in this country, we now abandon any serious attempt to classify the mentally subnormal by *grade* of mental defect. The term "severe subnormality" seems likely to be applied to patients whose condition varies from profound idiocy to the milder grades of feeble-mindedness. This may, as your correspondents say, have regrettable implications for clinical practice. It will also mean the end of much serious epidemiological research—just at a time when it is beginning to produce fruitful results. Not only will it be impossible to compare our experience in the future with what it was in the past, but we shall be unable to relate what is happening in England and Wales to what is happening in other countries dealing with similar problems. Again, the new terminology cuts right across the educational criteria of mental subnormality, by lumping together those educationally subnormal persons who later come to be in need of care with the lower-grade defectives who in childhood are excluded from the educational system. Prospective studies will thus be difficult to carry out.

Perhaps the best way out of the difficulties likely to arise from the new terminology would be to insist that for statistical and record purposes the terms "subnormal" and "severely subnormal" are always qualified by an I.Q. rating. If possible such ratings should be based on scores obtained on properly administered intelligence tests. But even a clinical judgment, expressed in deciles (I.Q. 40–49, 60–70, &c.) would be better than nothing.

The value of I.Q.s for statistical purposes is extremely great, as can be easily demonstrated:

(1) Whereas perhaps only 10% or fewer of adults with I.Q.s of less than 50 are able to be employed on the open market, at least 80% of those with I.Q.s of over 50 are fully employable.

(2) The cut-off point for employability, as for educability and marriageability, is 50+ rather than 60 or 70, as has been shown by Ferguson in his studies of Glasgow school-leavers, as well as by many others.

(3) Even within the imbecile grade there is a sharp gradient of educability. A recent American study by Goldstein of the "lower limits of eligibility for classes for trainable (i.e., imbecile) children" showed that the I.Q. was the most important single determinant of educability in the training centre. 15 out of 16 children with I.Q.s below 25 (94%) were excluded from the training centres during the course of his investigation. Only 6 of the 55 children (11%) with I.Q.s between 25 and 34 and 1 out of 45 children (2%) with I.Q.s over 35 were so excluded. Neither clinical diagnosis, mental age, nor Vineland social maturity score had such discriminatory power.

(4) There are immense differences between idiots and imbeciles in the management problems they present, and in expectation of life. Staff requirements and institutional accommodation for the various grades are very different, as is the average time that high-grade and low-grade patients require institutional care.

For all its shortcomings—many of which are well-recognised by psychologists who have been indefatigable

in drawing attention to them in recent years—the I.Q. remains one of the most powerful diagnostic tools we have in psychiatry and in education. If we are to give up the traditional grading of mental defect, as it seems we must, let us hang on to intelligence quotients until something better turns up to replace them.

Institute of Psychiatry,
Maudsley Hospital,
London, S.E.5. J. TIZARD.

"WHAT IS WRONG WITH ME?"

SIR,—Nearly every patient who feels ill or has some symptom says to himself or herself "I wonder what is the matter with me?" Frequently they ask their family doctor, who possibly replies "Oh, it is only a bit of flu," or a "touch of catarrh" or "rheumatism", and the patient is satisfied.

If, however, the patient is sent to the hospital, the position is very different. The patient still asks himself "what is the matter with me?" but very seldom has the courage to ask anybody. The atmosphere here seems to be that of the old nurseries, "ask no questions and you will hear no lies." How often one hears a patient just out of hospital, to whom one makes sympathetic noises, and asks what was the trouble, say, "Oh I don't know, they never tell you anything in hospital." Many of these patients go on worrying, particularly if they suspect rightly or wrongly that the condition was cancer. One patient in hospital the other day said to a visitor, "I know I have cancer but they won't tell me," and then, turning to the ward sister, said "why won't you confirm it?" The sister is reported to have replied, "The nurses are not allowed to discuss ailments with the patients." That may or may not be a good rule, but it should be the duty of *someone*, houseman or registrar, to tell *every patient* in lay language before leaving hospital what was wrong with him or her. This is an important part of the treatment.

Very seldom will a "white lie" have to be told, but if it is the "lie" should be passed on to the G.P.

"Knowledge is the antidote to Fear."—Emerson.

MALCOLM DONALDSON
Honorary Secretary,
Oxford. Cancer Information Association.

AGRANULOCYTOSIS ASSOCIATED WITH IMIPRAMINE

SIR,—Imipramine has come to be regarded as a valuable drug in the treatment of depression. Side-effects have not been unduly troublesome but agranulocytosis has been reported twice.[1 2] A patient recently treated with imipramine at the Maudsley Hospital developed agranulocytosis from which she recovered.

A woman of 70 was admitted to the Maudsley Day Hospital on May 17, 1960, with a depressive illness. Treatment with imipramine ('Tofranil', 25 mg. b.d.) was started on May 19, and she was also given 0·1 g. quinalbarbitone at night occasionally, as required. Four days later nausea and dizziness developed with a temperature of 99·4°F., for which no cause could be found. The blood-count at that time was entirely normal. Imipramine was stopped on May 27, but as the symptoms continued she was admitted to the ward under the care of Dr. Felix Post, where they gradually subsided.

On June 9 treatment with imipramine was started again, the dose being increased to 75 mg. t.i.d. She again received occasional doses of quinalbarbitone 0·1 g. as required. The depression lessened, but after six weeks she began to complain of profuse sweating, and the dose was reduced to 50 mg. t.i.d. A week later, on July 25, she complained of a severe sore throat. The throat was very red, without exudates or ulceration, and the cervical glands were tender on both sides. Her temperature was 98°F, but had risen to 100°F next day. The total white-cell count was 1100 per c.mm. (neutrophils 4%, lymphocytes 92%, monocytes 4%) and the hæmoglobin was 14·4 g. per 100 ml. All drugs were stopped at once, and she was treated with penicillin and cortisone. She made an uninterrupted recovery, and on the succeeding four days white-cell counts were 1200 (neutrophils 3%), 2100 (neutrophils 7%), 3100 (neutrophils 16%), and 9150 (neutrophils 63%) per c.mm. Over the next two weeks there was a neutrophil leucocytosis, with the total count rising to 27,000 per c.mm., but since then the count has remained normal. Her depression has now improved and she was recently discharged from hospital.

The only drug this patient received, apart from imipramine, was quinalbarbitone, and the doses of this were small and infrequent. Imipramine resembles in structure compounds of the phenothiazine group which are known to produce agranulocytosis and it would seem to have been the cause in this patient.

Maudsley Hospital,
London, S.E.5. SAMUEL I. COHEN.

1. Morgan-Hughes, J. A., Heald, I. N. S. *Lancet*, 1960, i, 552.
2. Bird, C. E. *Canad. med. Ass. J.* 1960, **82**, 1021.

CHEST X-RAYS AND RADIATION HAZARDS

SIR,—In 1957 the Ministry of Health issued a publication [1] on the development of the mass miniature radiography service and in 1959 a further memorandum [2] on radiological hazards to patients, which held that the value of mass radiography was so great that it should not be curtailed without good cause. The radiation distributed by these X-ray machines was considered to make a negligible contribution to the total radiation to which the populace is exposed. This statement is true, but although one can be reasonably sure there is little immediate hazard, the effect of small doses of radiation may have genetic consequences in the future. In an atomic age the amount of unavoidable radiation that the populace receives will probably increase as time goes on. Accidents similar to that at Windscale may happen again. All radiation is dangerous, and it is the duty of those concerned to see that all unnecessary radiation is avoided. What then of the future of the mass radiography using 35 mm. camera units?

The report on radiological hazards to patients quotes figures for the number of cases of tuberculosis found by this means in the whole of Great Britain in 1957 as a reason for continuing its use. These figures were not further subdivided into areas, but it is obvious that the bulk of the cases came from the large cities.

The same report also quotes the number of people X-rayed, and such figures have always been used to impress lay committees successfully. These same committees should now be re-educated to realise that it is the results that matter and not the numbers X-rayed. The successful unit is the one that can demonstrate how few people they have X-rayed to discover an appreciable number of new cases of tuberculosis. It is unrealistic to try to justify the continued use of M.M.R. units solely because of abnormalities other than tuberculosis. Even as a measure to discover new cases of tuberculosis, it is relatively expensive and will become more so in the future. In comparatively healthy areas 35 mm. units could successfully be replaced by static and/or mobile 70 or 100 mm. units mainly for the use of cases referred by general practitioners. Crofton [3] felt that 35 mm. camera units could still fulfil a useful purpose, but should be used less haphazardly. Even in Edinburgh, however, the time will come when their use will have to be reconsidered.

In some areas fluoroscopy sessions are used for the purpose of diagnosing chest disease. This should be condemned out-

1. H.M. (57) 94.
2. H.M. (59) 46.
3. Crofton, J. *Brit. med. J.* Sept. 3, 1960, p. 679.

right. The amount of radiation disseminated by each examination will vary considerably, but in any event will be substantially greater than the controlled dose given by radiography. Gibson [4] considered that routine fluoroscopy was no longer justified in the diagnosis of cardiac disease, owing to the high radiation dosage. It is even less justified as an initial means of diagnosing chest disease.

Finally, the use of chest X-rays in clinics could be reduced in certain cases. Children examined as contacts should not be X-rayed if their tuberculin test is negative. During pregnancy it is doubtful whether a routine chest X-ray is justified in the absence of symptoms; it could be delayed until the puerperium. The intervals for the routine surveillance of quiescent cases should also be reviewed at each attendance.

Quite obviously the extent by which irradiation can be reduced will vary in each area, but it is the concern of everyone to give the matter adequate thought at frequent intervals.

Bournemouth. O. D. BERESFORD.

WORKING WIVES—AND THEIR CHILDREN

SIR,—Your annotation last week showed great insight into the mental state of professional women tied to the household for some years.

Could we not find some way in our profession to enable women to retain their skill during the years when their children are small, by making part-time work more readily available?

I have in mind clinical assistantships in outpatient departments or a scheme whereby general practitioners accepted trainee assistants on a regular sessional basis.

Such part-time work, with sufficient remuneration to cover a reliable baby-minder, would go a long way to maintaining clinical interest during the critical 5 to 7 years before the youngest in the family is at school, when more work could be undertaken.

If the shortage of doctors, predicted by Professor Lafitte within the next decade, is to be avoided one obvious solution would surely be to make the fullest use of available part-time workers.

London, S.W.14. SYBILLE STOVIN.

SHORTAGE OF DIETITIANS

SIR,—I wonder if the recent King Edward's Hospital Fund memorandum on the shortage of dietitians, discussed in your annotation of Sept. 17, has received the notice it so urgently deserves. Those who read it will rightly regard it as a useful, though only preliminary, report and a balanced stimulus to more official action on this important subject which becomes increasingly related to many branches of modern therapy. The Professions Supplementary to Medicine Act may have a similar effect, though at first it seems to be mainly concerned with problems of registration, administration, and disciplinary procedures—with training facilities, &c., as mere afterthoughts.

Until recently the subject of dietetics seems to have escaped the attention of the Ministry of Health; and many doctors, both within and without the hospital service, have regarded this attitude as unrealistic.

Today the trained dietitian is quite often employed in the hospital service as a glorified cook with a not dissimilar rate of remuneration; and the reasons for this are probably (1) the present serious lack of trained dietitians; and (2) an incomplete knowledge of the subject by hospital staff.

4. Gibson, R. Cardiac Problems for Chest Physicians; p. 13. N.A.P.T. Symposium, London, 1958.

The answer lies in the provision of adequate and well-considered training in dietetics throughout the country, and the present situation seems sufficiently serious to justify the setting up of a small body of inquiry to examine the present arrangements for the training of dietitians—which I suggest are appalling—and also the whole question of their employment, including remuneration and status. I suggest that the King Edward's Fund memorandum could form a most useful basis for any such inquiry.

London. J. SHARP GRANT.

*** A note about a Ministry memorandum on the duties of dietitians and the organisation of their work appears on p. 1202.—ED. L.

BROADER MEDICAL TEACHING

SIR,—I was much interested in Dr. Cardew's letter of Nov. 5 and subsequent correspondence because the subject is one which has always been very near to my heart and on which I have written a good deal.[1]

During the past twelve months, as a patient in a regional hospital and then a teaching hospital, I have been able to talk, at night, with many recently qualified men, and all of them expressed the same opinions as the general practitioners at the conference.

Surely the basic training during the clinical years is misdirected in aim, structure, and balance? Its general purpose should be to teach the student the general principles of medicine; to train him to a sufficient degree of skill to diagnose and treat common ailments in medicine and surgery, and to recognise conditions in which expert help is required; and so to orientate his attitude toward medicine that he can see the picture as a whole. He will quickly learn to look for aberrations from normal as they present themselves, and realise the importance of training his powers of observation on each case as it occurs. Then he will find out that taking a very careful history is the best way of coming to a sound conclusion.[2]

But today, in his clinical ward rounds and ward work generally, he is introduced to the patients of a *teaching hospital* where his mind is largely absorbed with the rarities of medicine. Now that several teaching hospitals have branches which are staffed like the central hospital but contain the everyday type of case, would it not be possible for the student's clinical and ward work to be undertaken at these branches, with visits to the main hospital weekly for instruction in the rarities? At present students get a completely false picture of the world outside—the world of the commonplace in which they are to spend their working lives.

Again, under present arrangements students are taught almost entirely by members of the hospital staff whose lives are spent almost entirely in their own specialty (which cannot conduce to a broad outlook). Is this really the best plan? Is there not much to be said for forming a school in the art of teaching, or for asking the universities to recommend men of outstanding ability in this field (with suitable remuneration) whose words would ring in the minds of students throughout their lives? In this connection the foundation of a department of general practice in teaching hospitals, as is done in the United States and Canada, has much to recommend it.

Dr. Cardew suggests that every teacher in the hospital service should spend a period in general practice first. I would go further and say that no doctor should be allowed to specialise without first doing a period outside hospital in general practice. The time to do this is immediately after qualification and registration: it would be very unsound to postpone the experience till later. The modern tendency in medicine, or nursing, is to think of patients

1. Your Doctor of the Future. High Wycombe. 1953. State Medicine or What? London. 1952.
2. Hunt, J. H. *Brit. Med. J.* 1957, i, 1076.

as case-numbers instead of *souls* (human entities) which is unfortunate if doctors of the future are to hold the same position of love and trust as did their forebears.

Worthing. HAROLD LEESON.

"ATHEROLIPID NUMBERS": AN EXPRESSION OF SERUM-CHOLESTEROL AND SERUM-LIPOPROTEIN RELATIONSHIPS

SIR,—Increases in serum-total-cholesterol and serum-beta-lipoproteins have been associated with clinical manifestations of atherosclerosis. In addition, several investigators [1 2] have observed absolute as well as relative decreases in alpha-lipoproteins in sera from atherosclerotic patients. A consideration of these three lipid fractions may have clinical significance in this disease process. Therefore, a mathematical relationship has been derived which is dependent upon concentrations of serum total, alpha-, and beta-lipoprotein cholesterol. The value obtained from

$$\frac{\text{mg. per 100 ml. serum-total-cholesterol} \times \dfrac{\text{mg. per 100 ml. beta-lipoprotein cholesterol}}{\text{mg. per 100 ml. alpha-lipoprotein cholesterol}}}{10}$$

has been termed the "atherolipid number".

Calculation of atherolipid numbers does not include a factor which ascribes greater significance to any one of the lipid fractions. The divisor 10 has arbitrarily been used in this expression merely to limit the number of significant figures.

To study the proposed relationship, serum-total-cholesterol as well as alpha- and beta-lipoprotein levels have been estimated eletrophoretically by the technique of Searcy et al.[3] in over 1000 clinically healthy individuals. This group included 554 males and 529 females ranging in age from 10 to 79 years. Lipid values as well as ages were averaged for each decade. Fig. 1 demonstrates the effect of both sex and age upon serum-lipoprotein-cholesterol levels.

In males there is a big rise in the serum total and beta-lipoprotein cholesterol in the third and fourth decades. Females

1. Barr, D. P., Russ, E. M., Eder, H. A. *Amer. J. Med.* 1951, **11**, 480.
2. Oliver, M. F., Boyd, G. S. *Brit. Heart J.* 1955, **17**, 299.
3. Searcy, R. L., Bergquist, L. M., Jung, R. C., Craig, R., Korotzer, J. *Clin. Chem.* (in the press).

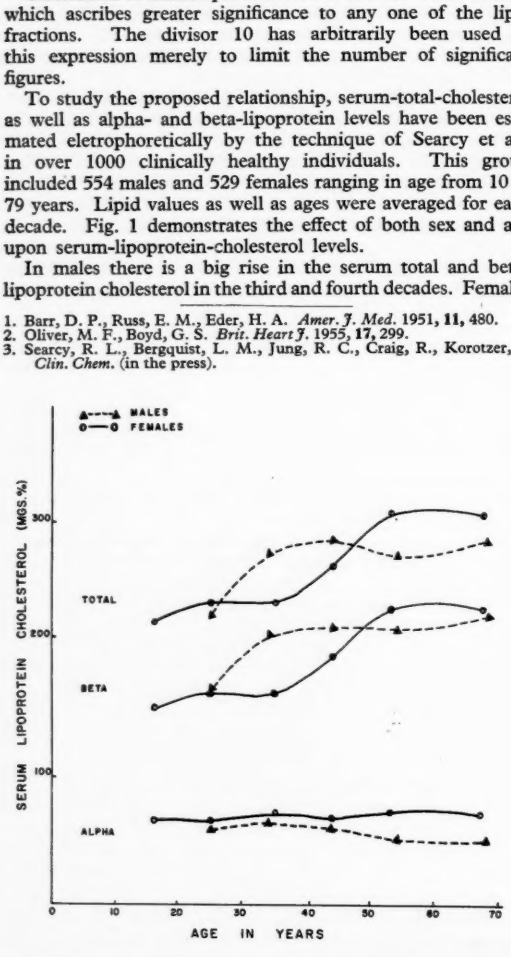


Fig. 1—Serum-lipoprotein-cholesterol levels in clinically healthy individuals.

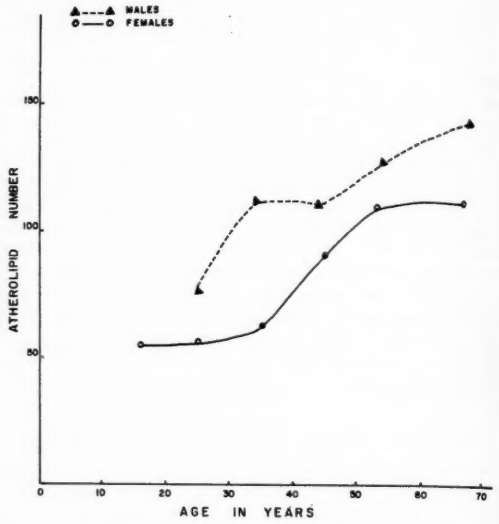


Fig. 2—Atherolipid numbers in clinically healthy individuals.

of corresponding age exhibit much smaller increases in these fractions. It is noteworthy that in the post-menopausal decades, females averaged a higher serum-total and beta-lipoprotein cholesterol than males of the same age. Oliver and Boyd[4] observed substantial increases in total cholesterol levels in 12 females aged 50–59 years as compared to both younger and older women. In contrast, our studies employing a larger number of subjects failed to demonstrate a drop in serum-total-cholesterol levels in the post-menopausal decades. A group of 69 women 60 years and over had an average serum-total-cholesterol of 302 mg. per 100 ml. compared to a mean of 304 mg. per 100 ml. in 74 females aged 50 to 59 years.

Lipid values obtained from the total study group have been used to calculate atherolipid numbers for subjects categorised according to sex and mean age. Fig. 2 shows that on the average atherolipid numbers of males are higher than those of females at all mean ages. These data are in contrast to the lipoprotein cholesterol measurements, where females over the age of 50 had lipid values higher than males of corresponding age. Reductions in alpha-lipoproteins in men of this age tend to increase the beta- to alpha-lipoprotein ratio thereby resulting in higher atherolipid numbers. Such elevations in atherolipid numbers are consistent with the greater incidence of atherosclerotic complications in the male population and may suggest a possible relationship. In females atherolipid numbers do not reach a maximum until after the menopause. This peak again corresponds to the age at which women are more susceptible to myocardial infarction.

Barr [5] has reported serum-total-cholesterol and distribution of this lipid fraction between alpha- and beta-lipoproteins in a group of myocardial infarction patients. The average "atherolipid number" of 161 calculated from these data exceeds mean "atherolipid numbers" observed in our study group of clinically healthy individuals. Therefore, a consideration of serum-total-cholesterol in addition to alpha- and beta-lipoprotein measurements may aid in distinguishing atherosclerotic from normal subjects. The significance of atherolipid numbers in a variety of disease states is now under investigation in our laboratories.

Los Angeles County Osteopathic Hospital, College of Osteopathic Physicians and Surgeons, Los Angeles, and the Cardiovascular Research Center, Burbank, California.

R. L. SEARCY
V. P. CARROLL II
W. H. DAVIS
L. M. BERGQUIST.

4. Oliver, M. F., Boyd, G. S. *Brit. Heart J.* 1953, **15**, 387.
5. Barr, D. P. *Circulation*, 1953, **8**, 641.

PROGNOSIS AND ANTICOAGULANT PROPHYLAXIS AFTER CORONARY OCCLUSION

SIR,—I should like to congratulate Professor McMichael and Dr. Parry on their article of Nov. 5—how well they have disposed of long-term anticoagulant therapy in patients with coronary occlusion.

I believe that many physicians, like myself, are weak-minded, but few would care to admit it. We are weak-minded because we yield to the requests of our patients and their relatives and prescribe anticoagulant drugs. Relatives do not seem to mind if their loved ones die in my beds from a further coronary occlusion—and many of them do—provided they are having "blood-thinning drugs", but many questions have to be answered if these drugs have been withheld. Similarly, if patients die from a further cardiac infarction any time after discharge from hospital, it is the doctors' fault for not continuing with these fashionable drugs. The relatives say, "Smith next door is on these drugs and he is still alive, but my poor John has gone". Although without faith it is probable that some of us use these drugs occasionally for these reasons. We may have been weak and wandering like lost sheep between New York, Edinburgh, and The London Hospital, but McMichael and Parry have given us strength and courage to remain static and adopt one course of action.

For many years I have been teaching students that it is vitally important for patients with coronary occlusion to move their feet and legs at regular intervals and to do deep breathing exercises, and so to prevent phlebothrombosis and possible pulmonary infarction. These measures are active substitutes for anticoagulants. Some patients, however, are so fat, so stupid, or so stuporose that they will not do these exercises, and in these cases I believe anticoagulant therapy should be considered. Others are so ill, so shocked and hypotensive that they cannot move their legs and in these patients anticoagulants are perhaps necessary.

It is about time that we fully realised that anticoagulants cannot prevent *arterial* thrombosis. No-one can persuade me that anticoagulants can postpone death from a further coronary occlusion: I have witnessed too many deaths in patients whose prothrombin-times have been so perfect.

McMichael and Parry have stabilised our views in their notable contribution and I only hope that a comparable article on short-term anticoagulant therapy will soon be forthcoming so that the disposal of these fashionable drugs may be completed.

Cardiff. BYRON EVANS.

ODOUR OF POTASSIUM CYANIDE

SIR,—Professor Moncrieff's letter of Sept. 3 refers to two papers in 1953 reporting that solutions of potassium cyanide were apparently odourless to 18% of white Australian males [1] and to 25% of males of the Luo and Kikuyu tribes in Kenya.[2]

Some six years previously, Stock [3] stated that he too was insensitive to this odour, and indeed only 6 out of 11 workers in his laboratory could detect it. Other authors [4 5] suggested that 1 person in 2 or 4 in 5 could detect it, and Holmyard reported [6] that during 21 years at Clifton College, he examined some hundreds of boys and that approximately 3 out of 5 found an odour. I then tested 20 adult white males and 20 females with a newly opened bottle of potassium cyanide crystals. For each sex, 16 subjects reported an odour, but few non-technical persons recognised it.[7]

It therefore seems evident that a substantial proportion of a population is unable to detect this odour, characteristic though it is. Howe [8] found it wise to have a suitable assistant beside him in his laboratory to advise him of any escape of cyanogen gas. Professor Gatterman is reported [4] as having advised—in 1904—the smoking of a cigar to facilitate the detection of cyanogen. Sachs,[9] who is insensitive to the smell of cyanide in the normal way, smokes a cigarette and records a "very nasty taste" in the presence of cyanide or cyanogen gas.

There are now of course reliable instruments which can be used to monitor cyanogen or hydrogen cyanide gases, but their use is not always practicable—or even necessary in cases such as the above.

Winthrop Laboratories,
Newcastle upon Tyne. J. R. GWILT.

HEATSTROKE

SIR,—I was very interested in your editorial of Oct. 15, but would most certainly agree with Wing-Commander Mortimer (Nov. 5) that it is perfectly possible to treat severe hyperpyrexia successfully without elaborate equipment, and it would be very unfortunate if doctors suddenly faced with such a desperate emergency were to be inactive or delay treatment because of a feeling of futility with the resources they had.

In these circumstances the best method to reduce temperature does seem to be the encouragement of evaporation of artificial sweat at all costs.

While doing my National Service I was for a short time involved in the medical care of British Forces in the Jordan port of Akaba on the Red Sea. A relatively unacclimatised airman suddenly collapsed semi-conscious and delirious on the beach with heatstroke. He was immediately sponged all over with what must have been warm water from available water-bottles, and his colleagues and my R.A.M.C. orderlies fanned him vigorously with their towels to create a reasonably good air current. He was then moved by stretcher vehicle about a mile to a small Army Hospital where we had facilities by courtesy of the Jordan Arab Army. During the journey the sponging was continued and, of course, the air current supplied by the movement of the vehicle. Once in hospital it was possible to continue treatment more vigorously with a small electric fan and recovery, though slow, was thereafter uneventful.

Edinburgh. A. G. M. CAMPBELL.

PERITONEAL DIALYSIS IN SALICYLATE INTOXICATION

SIR,—Dr. Elliott and Dr. Crichton (Oct. 15) described the use of peritoneal dialysis in human salicylate intoxication, much as Ettledorf et al.[10] used it in the dog. The differences in the solutions account for the difference in the amount dialysed. Ettledorf et al., using albumin as a dialysing fluid, succeeded in their best experiment in removing 19% of the salicylate dose. Dr. Elliott and Dr. Crichton point out "in retrospect we had hoped to wash out salicylates by dialysis but we believe we accomplished more by providing available base as a vehicle for enhancement of renal excretion of conjugated glycuronide."

We felt there is no need for an extra dialyser if the patient's own dialyser (the kidney) could be exploited to its maximum.

In experiments on rabbits and dogs we used tris (hydroxymethyl) amino-methane (T.H.A.M.) (Abbott) by infusion to promote salicylate excretion. This buffer alkalinises urine and increases urine output. It has been used in the treatment of respiratory acidosis.[11] In a 7 kg. dog given 1875 mg. of salicylate intravenously (blood-level 59 mg. per 100 ml.), an excretion of 1232 mg. of salicylate in the urine was induced by an intra-

1. Kirk, R. L., Stenhouse, N. S. *Nature, Lond.* 1953, **171**, 698.
2. Allison, A. C. *Man*, 1953, **53**, 23.
3. Stock, J. A. *Chem. & Ind.* 1947, p. 262.
4. Francis, F. G. *ibid.* p. 325.
5. Unstead-Joss, L. G. L. *ibid.* p. 294.
6. Holmyard, E. J. *ibid.* p. 294.
7. Gwilt, J. R. *ibid.* p. 325.
8. Howe, J. L. *ibid.* p. 374.
9. Sachs, W. *ibid.* p. 358.
10. Etteldorf, J. N., Montalvo, J. M., Kaplan, S., Sheffield, J. A. *J. Pediat.* 1960, **56**, 1.
11. Brinkman, G. L., Remp, D. G., Coates, E. O., McCall Priest, E. *Amer. J. med. Sci.* 1960, **239**, 341.

venous infusion of T.H.A.M., and the serum-salicylate fell to 29 mg. per 100 ml. in four hours. The same animal, given another 1875 mg. of salicylate intravenously, put out 198 mg. of salicylate in the urine in four hours on a lactate-saline intravenous infusion, reducing the plasma salicylate from 55 to 41 mg. per 100 ml. This material is apparently non-toxic to humans and we intend to carry out clinical trials in salicylate intoxication.

Clinical Investigation Unit,
Children's Hospital of Winnipeg.

SYDNEY ISRAELS
HAROLD DAVIES.

LECTURES IN HÆMATOLOGY

SIR,—Your review (Nov. 5) of *Lectures on Hæmatology* states that the potential reader could "buy a whole textbook of hæmatology, containing nearly everything in this volume and a lot more, for rather less". In justice to the contributing lecturers I feel compelled, as editor of the volume in question, to point out that this statement is specifically untrue. The bulk of the material appearing in the lectures is not yet available in any current general hæmatological text with which I am familiar, certainly not in the texts of Whitby and Britton, Wintrobe, de Gruchy, Sturgis, Bernard and Bessis, Storti, Heilmeyer and Begemann, or Leavell and Thorup, and most of these works are, in any case, substantially more expensive.

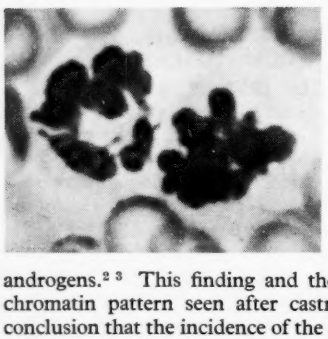
You go on to say that none of the illustrations in *Lectures on Hæmatology* are really necessary. This is a surprising comment since most of the line diagrams and half-tone plates serve either to replace, more clearly and economically, alternative detailed written descriptions, or to provide necessary illustrations of arguments put forward in the text.

Department of Medicine,
University of Cambridge.

F. G. J. HAYHOE.

EFFECT OF ANDROGENS ON NUCLEI OF NEUTROPHIL LEUCOCYTES

SIR,—When studying the influence of sex hormones on the incidence of the different sex-chromatin forms in leucocytes,[1] we found that after ten days of androgen treatment, the frequency of C forms, which usually number about 2–3% in infantile male rats, reached 12%, a value characteristic of the mature male. The incidence of forms A (drumstick) and B was not affected by the administration of androgens.[2 3] This finding and the changes of the sex-chromatin pattern seen after castration [3] led us to the conclusion that the incidence of the so-called pseudoforms was closely related to maturation—i.e., to an androgen effect.



After repeating and extending our experiments, we have now established that after a long period of androgen treatment the nuclear configuration of certain leucocytes also shows a characteristic change, in addition to the increased number of the pseudoforms C (small clubs, rackets).

The most conspicuous alteration is a focal condensation of the nuclear substance showing increased basophilia, which is clearly visible in smears stained with a Giemsa solution (see figure). There are usually several round or ovoid condensations in the nuclear substance, giving an indented appearance to the nuclear surface, resembling a blackberry or a bunch of grapes. These "blackberry" forms were later found not only in male animals but also in female rats treated with androgen and also in three female patients receiving intensive androgen treatment for mammary carcinoma.

Since these "blackberry" forms could not be observed after treating rats of either sex with œstrogen, progesterone, or cholesterol, we believe that they may be regarded as a morphological sign of an increased androgen level.

Department of Pathology,
Medical University,
Pécs, Hungary.

CH. MÉHES
ST. ZSIFKOVITS
C. JOBST.

NEPHROPATHY DURING PHENINDIONE THERAPY

SIR,—Toxic effects due to phenindione used for short-term or long-term anticoagulant therapy are rare. The commonest forms are fever, rash, and agranulocytosis. Jaundice has also been reported,[1 2] and so has prolonged and severe diarrhœa with steatorrhœa.[3] A case of agranulocytosis complicated by proteinuria and uræmia was described by Kirkeby.[4] Most reports of renal damage have been in the nature of hints, such as the case of Kirkeby, but two further cases have been recorded.[5 6]

The first of these was a case of dermatitis, hepatitis, and nephritis during phenindione therapy. The renal features were albuminuria and granular casts with red and white cells in the urine.

Barritt and Jordan [6] describe a fatality during treatment of pulmonary embolism with phenindione. Renal tubular necrosis was assumed to be due to the anticoagulant drug. Fever and diarrhœa were present, with oliguria, anuria, and raised blood-urea. Necropsy showed extensive tubular necrosis.

The following example of diarrhœa and nephrotic syndrome arose during "long-term anticoagulant therapy" with phenindione.

In 1959 a professional man of 59, previously of good health, had a myocardial infarct, for which he was treated with phenindione. Treatment was continued after the first month in doses sufficient to keep the prothrombin at a "therapeutic level". The dose averaged 50 mg. to 75 mg. per day. The patient had 6 weeks' holiday after convalescence. During the last 3 weeks he had severe diarrhœa, which did not respond to any remedy. He continued to take his phenindione.

After 2 weeks of diarrhœa his legs began to swell, and became progressively worse. The hands were involved to a less extent. At this stage he was admitted to hospital. Massive œdema of legs and thighs was present, with ascites and bilateral pleural effusions at the bases. No rise in venous pressure was present. The heart was clinically normal; blood-pressure 140/80 mm. Hg. There were no retinal changes. The urine was loaded with albumin and contained hyaline casts. The serum-electrolytes were normal; the blood-urea was 52 mg. per 100 ml. and serum-cholesterol 200 mg. per 100 ml. The peripheral blood-picture was normal. The stools contained no pathogens or occult blood, and their fat content was normal.

The diarrhœa was regarded as due to phenindione, and the drug was immediately stopped. The diarrhœa lessened, and ceased after 4 days. None of the known causes was found for the "nephrotic syndrome", and it was strongly suspected that this was also due to phenindione.

Treatment with prednisone 30 mg. a day resulted in a gradual diuresis and general improvement. The pleural effusions and ascites absorbed, and the legs were free of œdema in 4 weeks. The serum-albumin level improved, but the albuminuria persisted in varying but considerable quantities.

1. Jobst, C., Zsifkovits, S., Méhes, C. *Endokrinologie* (in the press).
2. Pfeifer, G. *Zbl. Gynäk.* 1960, **82**, 220.
3. Zsifkovits, S., Méhes, C., Jobst, C. *Nature, Lond.* 1959, **184**, 1239.

1. East, E. N., Beamish, R. E. *Canad. med. Ass. J.* 1957, **77**, 1028.
2. Burns, C., Desmond, F. B. *N.Z. med. J.* 1958, **57**, 283.
3. Juel-Jensen, B. E. *Brit. med. J.* 1959, ii, 173.
4. Kirkeby, K. *Lancet*, 1954, ii, 580.
5. Brooks, R. H., Calleja, H. B. *Ann. intern. Med.* 1960, **52**, 706.
6. Barritt, D. W., Jordan, S. C. *Lancet*, 1960, i, 1309.

The patient has continued in good general health on continuous prednisone therapy in smaller dosage. This was gradually reduced to as little as 5 mg. a day for 5 days a week, but this resulted in swelling of the feet once more. Between 5 and 10 mg. daily seems to be sufficient for control, but has had no appreciable effect on the albuminuria. The patient is now fully employed, and feels well in every way.

The 3 weeks' uncontrollable diarrhœa ceased within a few days of stopping phenindione. It is reasonably clear that this feature was due to the drug, and was similar to that described by Juel-Jensen. It seems reasonable also to blame the drug for the nephropathy. Renal damage has been described previously during administration of phenindione. Observation of the patient for 10 months has revealed none of the usual causes of the nephrotic syndrome. For this to arise from some other cause during the period of a recognised toxic feature (diarrhœa) seems unlikely coincidence. The evidence for renal damage disappeared after stopping the drug in Brooks and Calleja's patient. Recovery might have occurred in this case had the drug been stopped at the first sign of toxicity. It seems that persisting with the drug during the period of diarrhœa led to permanent renal damage.

Other anticoagulants have been used less extensively perhaps, but so far do not seem to have been responsible for such grave toxic effects. It seems desirable to use one of the alternative preparations, or to keep a close eye on the urine for albumin during phenindione therapy.

Dewsbury General Hospital, Yorkshire. GODFREY B. TAIT.

TYPE-14 ECHO VIRUS AND INFANTILE GASTROENTERITIS

SIR,—In July, 1959, three babies in a nursery had gastroenteritis with bloody stools. From rectal swabs 13 strains of Echo virus type 14 were isolated in the three children and in twenty contacts. This virus has occasionally been isolated in sporadic infantile diarrhœa,[1] but here it was epidemic. Such an epidemic, but due to Echo virus type 18, was recorded in premature babies in 1958.[2]

On July 19, two infants, 9 and 14 months old, suddenly developed symptoms of gastroenteritis with fever, dehydration, and bloody stools. The same syndrome appeared 48 hours later in a third child of 16 months. All three recovered after rehydration in 5 to 8 days. Stool cultures showed no pathogenic bacteria: no shigella, no salmonella, or any of the serological types of *Escherichia coli* usually isolated in infantile gastroenteritis. Inoculation of rectal swabs on primary cultures of monkey-kidney cells from *Cynocephalus babuin* induced the cytopathogenic effect of enteroviruses. The three strains did not grow, at first passage, on primary human amniotic cells. They showed no effect on KB cells. They were not pathogenic for suckling mice.

They were neutralised by an antiserum prepared in rabbits with the Tow reference strain of Echo virus type 14. There was no neutralisation with Echo antisera 1–13 kindly supplied by the National Foundation for Infantile Paralysis.

By rectal swabs 10 other strains of Echo virus type 14 were isolated from twenty children living in the same nursery. Among the non-carriers two showed serological evidence of infection. The carriers had no symptoms or signs except for a stationary weight for three or four weeks.

The sera of the three patients were challenged by seroneutralisation against 100 T.C.D.$_{50}$ of Echo virus type 14. Two of them had a significant rise in antibody between acute and convalescent sera, from none to a titre of 1/40. The third patient developed no antibodies; the virus was present in the fæces for at least three weeks, after which the child could no longer be followed.

Seven of the ten healthy carriers, studied at different times, had neutralising antibodies in their sera.

This survey shows that Echo virus type 14 can be highly contagious in a nursery. Infection by this virus may be manifested in infants by gastroenteritis.

Institut Pasteur, Paris. P. LEPINE.
J. SAMAILLE
J. MAURIN
O. DUBOIS
Institut Pasteur, Lille. M. C. CARRE.

1. Ramos-Alvarez, M., Sabin, A. B. *J. Amer. med. Ass.* 1958, **167**, 147.
2 Eichenwald, H. F., Abadio, A., Arky, A. M., Hartman, A. P. *J. Amer. med. Ass.* 1958, **166**, 1563.

GONADAL DYSGENESIS (TURNER'S SYNDROME) WITH MALE PHENOTYPE AND XO CHROMOSOMAL CONSTITUTION

SIR,—It is a pity that Dr. Bloise and his colleagues (Nov. 12) described their patient under the primary heading of Turner's syndrome. This was originally described in females and embodies various characteristic clinical features. When the XO chromosomal constitution was demonstrated in 1959 by Ford and his colleagues, they emphasised again that the patients were female but had an abnormal genotype.

Dr. Bloise's patient has a male phenotype and apparently none of the clinical features of Turner's syndrome. The diagnosis seems to rest entirely on the XO chromosomal constitution. If, as this case suggests, there may be other syndromes associated with an XO constitution, would it not prevent future confusion to reserve the diagnosis of Turner's syndrome for females who show the clinical features of it?

Cambridge. LAURENCE MARTIN.

CHILD'S OVERHEAD FRAME

SIR,—The accompanying illustration shows an overhead frame for the treatment of fractures of the shaft of the femur, and of burns of the buttock, by the gallows method in children below the age of five. This frame can

be adapted to suit any size of child's cot. There are no protruding nuts and bolts to be undone by other children in the ward, and the frame can be erected in a matter of minutes by the nurse. The screws are countersunk, are not amenable to damage, and cannot be undone without the use of the special key provided.

This frame has been made for me by the London Splint Co., 69, Weymouth Street, London, W.1.

Guy's Hospital, London, S.E.1. G. A. MARIN.

POSTPARTUM PRE-ECLAMPSIA

SIR,—I have read Mr. Theobald's letter in your issue of Nov. 19. The homœostatic changes characteristic of toxæmia affect the solvent (water) and the electrolyte (sodium). The evidence I have already adduced incriminates a predominant mechanism in their production—a diversion of the renal circulation causing ischæmia of the cortex. An action of the tubules brought about by hormonal influences cannot be held primarily responsible for these changes.[1]

The obstetrician must not be beguiled into believing that toxæmia is anything but a single entity by the fact that pregnancy can occur in association with acute or chronic glomerular nephritis, nephrosis, essential hypertension, phæochromocytoma, beriberi, cerebral hæmorrhage, or any other incidental and recognisable disease.

Worthing. JOHN SOPHIAN.

A MASSIVE OVARIAN CYST

SIR,—In a competitive spirit, I should like to report an enormous ovarian cyst. It may be surpassed in weight alone, but I shall be surprised if it can be beaten as regards the ratio of weight to body-weight.

A Fijian woman, aged 32, was admitted to this surgical unit in July, 1959. Since the birth of twins 2 years before she had noticed a symptomless lower abdominal swelling, which had enlarged at a uniform rate until 3 months before admission to hospital. It had then grown more quickly, becoming associated with malaise and discomfort from the increased weight and size (see figure). The patient's weight was 250 lb.

An ovarian cyst was the obvious diagnosis, but the appearance was not much different from the massive leiomyoma reported by Clinton-Thomas.[2] An intravenous pyelogram was therefore arranged, but, as the renal outlines could not be demonstrated on the preliminary plain film, the examination was abandoned (Dr. H. E. Knowles).

At operation through an incision running from the xiphisternum to the symphysis pubis, a way into the peritoneal cavity was found just below the xiphisternum, and the abdomen was opened through its length. There were adhesions—some quite thick—between the cyst and the parietes. When these were divided carefully, the massive cyst was traced down to the left fallopian tube, the pedicle being about 2 in. wide. After removal of the cyst a superabundance of abdominal wall remained. After dissection well back off the recti, a large amount of skin was excised, and the recti were then overlapped completely throughout their length. This tightened up the abdominal wall fairly well.

Postoperative progress was uneventful; the patient's general condition improved, and her weight after operation was 103 lb.—indicating that the cyst weighed about 147 lb. As an outpatient a month later her weight was 109 lb.

The histopathological report (Dr. M. E. Gosden) read: "Fibrous-tissue wall lined with a single layer of cuboidal epithelium. There is no evidence of malignant change."

When seen in May, 1960, the patient's weight was 130 lb., and she felt particularly well. The abdominal wall had tightened up appreciably although there was still some slack skin.

This case shows the harmful effect of pressure alone, as indicated by the calculated weight-loss. The precise explanation is uncertain, although presumably pressure on vital organs—thoracic and abdominal—played an important part.

I wish to thank Dr. P. W. Dill Russell, C.B.E., director of medical services for Fiji, for permission to publish this case-report.

Lautoka Hospital,
Lautoka, Fiji. J. M. FOREMAN.

LOCAN PESSARIES IN THE TREATMENT OF TRICHOMONAL VAGINITIS

SIR,—Certain points in the interesting paper by Dr. Eckersley and his colleagues (Sept. 3) deserve comment. For example, that anything less than two 'Locan' pessaries in 24 hours would not be expected to be effective.[1] When this was given, their results with locan were identical with those obtained with the control, acetarsol. It is inferred that acetarsol is much less toxic than locan, but how far is this from the truth? In the past few years many reports of serious toxic effects of acetarsol pessaries have appeared; these include frequent vomiting, purpura and other rashes, encephalopathy, and unconsciousness, in addition to one fatal poisoning.[2–5] One cannot avoid the conclusion that acetarsol is such a toxic substance compared with any of those in locan that its use should be avoided when another equally or more effective preparation is available which does not cause such dangerous complications. In spite of this, they recommend that locan should not be used on the grounds of sensitisation and reaction.

This view was supported by Dr. Scott-Gray (Sept. 17), who quoted her colleague, Dr. Marjorie Murrell.[6] With reasonable results from any drug, we cannot hope to get away from personal preferences in its use. The evidence for the side-effects referred to by your contributors was not supported by our own observations. In Murrell's short series, 3 cases of eczema of the vulva were encountered, but there was no evidence that this was due to sensitisation to any of the ingredients of locan, local anæsthetic or other. In a case of our own, there was at first discomfort but treatment was persisted in and as the lesion improved, this initial effect disappeared. In Dr. Eckersley's series, there seems to have been 1 true case of allergic sensitisation; in the remaining 4, treatment was stopped immediately. Only the first of the 5 cases had a rash, suggesting true allergy, but the application of local anæsthetics to other mucous membranes, such as the eye, can cause initial discomfort until the surface is anæsthetised.

Like ours, theirs was a satisfactory trial, and the fact that the time and frequency of relapses were the same for each preparation, shows that the population treated was similar in each instance.

The paper by Dr. Eckersley and his colleagues supports recent symposia and the paper by Catterall and Nichol[7] which have emphasised the need to treat both partners if relapse is to be avoided. It may well be that the results from treatment with locan and acetarsol are the maximum that can be obtained until this can be achieved.

Owing to improved formulation the activity in locan against trichomonas and other pathogens has recently been increased by a factor of 40 without any increase in the amounts of the

1. Sophian, J. *Lancet*, Nov. 12, 1960, p. 1086.
2. Clinton-Thomas, C. L. *Brit. J. Surg.* 1956, **43**, 497.

1. Stewart, H. C., Hughes, W. H., Thomas, E. G., Nixon, W. C. W. *Lancet*, 1957, ii, 1028.
2. White, A. *Brit. med. J.* 1956, ii, 1528.
3. Pearson, A. *ibid.* 1957, i, 340.
4. *ibid.* July 16, 1960, p. 242.
5. Acheson, J. *ibid.* Aug. 20, 1960, p. 603.
6. Murrell, M. *Lancet*, 1957, ii, 1285.
7. Catterall, R. D., Nichol, C. S. *Brit. med. J.* 1960, i, 1177.

active ingredient, which should reduce the time of exposure necessary to the allegedly sensitising chemicals, or enable a reduction in their amount.

Although we cannot agree with the conclusions drawn, we are glad that they have been contradicted by the data quoted in the body of the paper which so well support the efficiency of locan treatment.

Departments of Pharmacology and Bacteriology, St. Mary's Hospital Medical School, London, W.2.

H. C. STEWART
W. HOWARD HUGHES.

TREATMENT OF TENSION PNEUMOTHORAX

SIR,—The immediate treatment of tension pneumothorax seems still to be widely misunderstood by those who see this condition in its early stages. The necessity for continuous pleural decompression is appreciated but the method commonly used to achieve this is inefficient and dangerous. An emergency not infrequently seen by the thoracic surgeon is the patient, bloated with surgical emphysema and gasping for breath, with that anachronism "the indwelling needle" dangling uselessly from his chest. Any needle from lumbar puncture to French's transfusion seems to be used. All, even including Foster-Carter's which was designed for the purpose, are inefficient, uncomfortable, and dangerous.

The objections to the use of a needle are threefold:

(1) Whatever its size, by its very nature, a needle cannot be big enough to cope with the large volumes of air coming from a major leak. The insertion of a needle brings immediate, but temporary, relief. Air, however, cannot escape fast enough, pressures again rise, and air is forced into the tissues along the needle track. Soon the whole apparatus is floated out of the pleura into the chest wall as the skin lifts on a rising tide of surgical emphysema. Decompression ceases and the tension pneumothorax is re-established.

(2) Whether the point is sharp or blunt the rigid needle may puncture the lung as it expands—particularly the fragile tissue of bullous emphysema.

(3) A needle cannot be fixed satisfactorily into the chest. Adhesive tape, corks, perforated bottle caps, or plastic shields are some of the favourite methods. None is secure or comfortable.

The only safe way to decompress the pleural space is through a rubber catheter about size 10 Jaques inserted, usually, in the second intercostal space anteriorly. The technique is simple provided that the position for the catheter is checked by the preliminary aspiration of air. The tube is inserted through a stab wound with the aid of a trocar and cannula. A generous length is passed into the space, the catheter is attached to the skin and is then connected to an underwater seal. Such a tube will carry off large volumes of air, cannot slip out, will not damage the lung, and by its flexibility permits the patient to be moved in comfort. A similar tube can be used in an infant suffering from a staphylococcal tension pyopneumothorax.

I do not apologise for labouring a point that may be familiar to many. There are still too many patients whose lives are jeopardised and whose treatment is unnecessarily prolonged by the use of these inefficient methods.

Tension pneumothorax is usually a simple mechanical problem which will respond to the application of simple mechanical principles. The apparatus necessary for the insertion of an intercostal catheter should be part of the standard equipment on every medical ward.

Regional Thoracic Unit, Brook Hospital, London, S.E.18.

A. M. MACARTHUR.

Obituary

JAMES BURNETT RAE

M.B. Aberd.

Dr. Burnett Rae, who died on Oct. 31 at the age of 80, was for many years vice-chairman of the Churches Council of Healing, which, with the late Archbishop Temple, he helped to found. A few days before he died he was elected vice-president of the Council.

He was born in Edinburgh; but his father, the late John Rae, J.P., was an Aberdonian, and he was educated in Aberdeen. He graduated M.B. in 1902, but after postgraduate studies in theology at New College, Edinburgh, he spent several years as assistant minister at Sefton Park Presbyterian Church, Liverpool. Against this background, his service with the R.A.M.C during the 1914–18 war not unnaturally led him to share in the pioneer work on the treatment of functional and nervous disorders. He became consulting psychotherapist to Queen Alexandra's Hospital, Millbank, and medical officer in charge of the psychotherapy department at the Cambridge Hospital, Aldershot.

After the war he continued to work in this new specialty, and he was a member of the staff of the Croydon General Hospital and the Institute for the Scientific Treatment of Delinquency. He also lectured for the National Association for Mental Health. But his interest in pastoral therapy was the centre of his practice, and of this side of his life E. E. C. writes:

"Burnett Rae was a superb example of a man who practised what he preached. Not that he preached often, though he was always willing to occupy a pulpit on such occasions as Hospital Sunday, St. Luke's day, or a series of addresses on health and faith. He believed that Medicine and the Church have complementary tasks, and he strove to help Medicine to realise that its work was incomplete if the spiritual factor was omitted in treatment. He was always open to believe that God would and did intervene in the course of illness. So much, he used to say, occurs which we cannot explain, let us therefore rejoice when a patient learns the vital secret of faith and his illness clears up. He himself once had a spot on the lung which he firmly believed resolved through prayer and his own faith. He believed that when he was examining his patients he was in fact 'laying on hands'—such was his approach. He was a wonderful raconteur and always had a fund of apt illustrations. He was also a good listener, and many found that just to talk to him did them good. A dear loving friend and truly a 'beloved physician'."

Appointments

BOLAND, MARY K., M.B., N.U.I., D.C.H.: assistant M.O.H., St. Helens, Lancashire.
CONSTABLE, F. L., M.D., B.SC.Durh.: consultant bacteriologist, Royal Victoria Infirmary, Newcastle upon Tyne.
HUGHES, J. T., M.B.Manc., M.R.C.P., D.C.P.: assistant neuropathologist (S.H.M.O.), Radcliffe Infirmary, Oxford.
ORR, J. M. B., M.B.: assistant M.O.H. and school M.O., Ipswich.
PEARSON, VERONICA, M.B. Cantab., D.OBST., D.C.H.: assistant M.O., Halifax.
WOODMANSEY, A. C., M.D. Leeds, M.R.C.P., D.P.M., D.C.H.: consultant in child psychiatry, Sheffield Regional Hospital Board and United Sheffield Hospitals.

Leeds Regional Hospital Board:

DAVID, J. D. P., M.D., B.SC. Wales: consultant in geriatrics, Pontefract and Wakefield area hospitals.
ELLETT-BROWN, HAROLD, B.M. Oxon., D.P.M.: consultant psychiatrist and deputy physician-superintendent, De la Pole Hospital, Willerby.
HAMILTON, MARGARET G., M.B. Belf.: S.H.M.O. in pathology, Harrogate area hospitals.
LAMONT, S., M.B., F.F.A. R.C.S., D.A.: consultant in anæsthetics, Leeds area hospitals.
NEWCOMBE, JOHN, M.B. Lond., D.P.M.: consultant in psychiatry and medical superintendent, York group of mental-deficiency hospitals.

Colonial Appointments:

BLACKMAN, VICTOR, M.B. Lond., D.P.H., D.C.P.: specialist (clinical pathologist), Uganda.
DOS SANTOS, W. A., M.B. Cantab., DIP.BACT.: government bacteriologist and pathologist, Barbados.
GEMMELL, W. R., M.B. Glasg.: D.M.S., Bechuanaland.
SANSOME, J. F., M.B. Lond.: M.O., B.S.I.P.
STEVENSON, MAUDE, M.D. Belf., D.C.H.: M.O., Bahamas.

Notes and News

SUPPLEMENTARY ESTIMATES

THE supplementary estimate for the National Health Service in the current financial year [1] shows an increase for England, Wales, and Scotland of £42,900,000, bringing the total net cost to £626,400,000. Of this, £41 million is needed to meet the increased remuneration for doctors recommended by the Royal Commission: £24 million is to cover arrears, and the balance of £17 million represents the cost of a year's increments.

DIETITIANS

THE Ministry of Health, in conjunction with King Edward's Hospital Fund for London, has lately surveyed the work of dietitians.[2] Suggestions for the more effective use of their specialised knowledge are contained in a memorandum[3] from the Ministry.

The dietitian should be relieved of unskilled work in order that she may act more as an adviser and instructor. Her duties should include drawing up diet sheets, calculating individual inpatient diets, compiling therapeutic diets with the catering officer, providing recipes for special dishes, training diet cooks, interviewing and instructing patients in wards and discussing patients' dietaries with ward sisters, advising catering officers on the nutritive value and suitability of menus, advising outpatients, assisting in teaching nurses and others, and performing any dietary surveys requested by the medical staff. Light, vegetarian, religiously determined, and some gastric diets do not need direct supervision by the dietitian, though she can assist in their planning. Menu planning by dietitians for the main catering in hospitals not only ensures that the dietary is appropriate but results in less work, as requests for special diets are fewer and use can be made of food from the main kitchen for therapeutic diets.

The present shortage of dietitians may make it necessary to employ one dietitian for a group of hospitals. The Ministry regards this, not as a temporary expedient, but as a logical development.

ORTHOPÆDICS AT OXFORD

Professor Trueta last December set himself what must have proved a satisfying task—that of reviewing orthopædics at Oxford up to the end of his first ten years as Nuffield professor.[4]

The first holder of this chair was G. R. Girdlestone, one of the band of men who became disciples of Sir Robert Jones before, during, and just after the first world war. It was Girdlestone who founded a regional orthopædic service at Oxford on the basis of a central hospital (the original "Wingfield") with peripheral clinics in the neighbouring towns, and this scheme has been a model for orthopædic services elsewhere in the country. Through his friendship with Lord Nuffield, he established what came to be known as the Wingfield-Morris Orthopædic Hospital with all its ancillary services devoted to the treatment, rehabilitation, and education of long-stay orthopædic patients.

Girdlestone was succeeded as Nuffield professor in 1940 by H. J. Seddon, who brought increased renown to Oxford orthopædics in his work, particularly on peripheral nerve injuries and poliomyelitis. In the few years after the war before he became director at the Royal National Orthopædic Hospital, surgeons from abroad had already become eager to work with him at the Wingfield-Morris.

In 1949 he was followed by Professor Trueta, under whose guidance the importance of research, not only in itself but as an integral part of the training of every orthopædic surgeon, has been given new impetus. With further help from Lord Nuffield, a great new building has appeared which houses the outpatient department, records office, radiological department, and lecture hall as well as the research laboratories and offices of the university department proper. Yet another baptism was called for, and the old Wingfield-Morris with the new buildings and extensions has become the Nuffield Orthopædic Centre.

1. 1960–61 Supplementary Estimate: Civil Estimates. H.M. Stationery Office. 1960. Pp. 9. 9*d*.
2. See *Lancet*, Sept. 17, 1960, p. 636.
3. H.M. (60) 91.
4. Lecture delivered by Prof. J. Trueta at the Nuffield Orthopædic Centre, Oxford, on Dec. 3, 1959.

Among Professor Trueta's interesting ideas for the future is that the Nuffield centre should be placed officially "at the disposal of the orthopædic specialists of the whole region, from consultants to junior staff". The consultants at the periphery should have opportunities at the centre, including charge of beds where they can study their cases of special interest with all the research facilities at their disposal and without the hurry and anxiety of overloaded clinics and emergency interruptions. The difficulty of obtaining junior staff in regional hospitals can, Professor Trueta thinks, be mitigated by a system of exchange for part of their time of service between those working in the periphery and the trainees at the centre itself. Only by increasing the attractiveness of such appointments in this way can we hope to stimulate the best men to enter on the long climb to surgical consultancy and reverse our increasing dependence on foreign aid to fill the junior posts in non-teaching hospitals.

MANCHESTER MEDICAL GAZETTE

THE *Manchester University Medical School Gazette* has marked the 62nd year of its existence by a change of title; its new name reflects its increasing circulation among graduates. In the first issue of the *Manchester Medical Gazette*,[1] devoted mainly to education, Dr. J. R. Ellis writes on "preparation for medicine as a profession" (an abridged version of his Wood Jones lecture, extracts from which we published in our issue of Nov. 12), Dr. R. F. L. Logan on "general practice tomorrow", and Mr. A. R. Anscombe on "clinical teaching"; and a thoughtful critique of the preclinical course is contributed by a medical student.

If the high standard of the first number is maintained, the *Gazette* will undoubtedly fulfil its aim of interesting Manchester students and graduates, and all the medical men practising in Manchester.

1. *Manchester Medical Gazette*, vol. 40, no. 1, October 1960. Edited by E. S. Rosen, B.Sc. Obtainable from the Medical School, The University, Manchester, 13. Annual subscription 10*s*. 6*d*.

University of Cambridge

On Nov. 12 the degree of M.B. was conferred on R. H. C. Vaux.

University of Leeds

On May 18 the honorary degree of D.SC. will be conferred on Prof. C. H. G. Macafee.

University of Aberdeen

Dr. Mary Scott has been appointed to a lectureship in physiology.

University of Wales

At recent examinations for the D.T.C.D. the following were successful:

Aftab Ahmed, J. O. W. Ang'Awa, Ghalam Azam Chowdhury, Panchkari Ghosh Dastidar, Chelliah Kulanayagam, Mankavil Kovilveetil Karunakara Menon, Jyothinagaram Thimmaraya Chetty Ramalingam.

Royal College of Surgeons of England

On Dec. 7, at 2.30 P.M., at the college, Lincoln's Inn Fields, W.C.2, Sir Stanford Cade will give a Bradshaw lecture. He will speak on Malignant Melanoma. On Dec. 8, at 5 P.M., Mr. H. J. Seddon will give a Robert Jones lecture. His subject will be the Manchester Ship Canal and the Colonial Frontier.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the Faculty on Nov. 7, the following officers were elected:

President, Dr. J. H. Wright; visitor, Prof. C. F. W. Illingworth; hon. Secretary, Dr. Gavin B. Shaw; hon. Treasurer, Mr. R. B. Wright; hon. Librarian, Dr. A. L. Goodall; representative on the General Medical Council, Prof. D. F. Cappell; representative on the General Dental Council, Prof. W. Malcolm Gibson; councillors, Dr. G. J. Aitken, Dr. W. Ferguson Anderson, Prof. Roland Barnes, Mr. Thomas Gibson, Dr. A. D. Telford Govern, Prof. T. Symington, Dr. T. J. Thomson.

Mohamed Abdel Kader Mansour was admitted as a fellow of Faculty *qua* surgeon. The Macewen medal was awarded to Dr. I. W. Young.

University of London

The following have passed the final examination for the M.B., B.S.:

Honours.—G. M. Besser (*b,d*), St. Bartholomew's; D. J. Galton (*b*), University College; Margaret L. Jones (*d*), St. Mary's; H. A. Lee (*c,d*), King's College; P. H. Millard (*d*), University College; Jennifer P. Peebles (*e*), Guy's Hospital; B. A. Senewiratne (*b*), University College.

(*b*) distinguished in medicine; (*c*) distinguished in applied pharmacology and therapeutics; (*d*) distinguished in surgery; (*e*) distinguished in obstetrics and gynæcology.

Pass.—R. O. Addae, Adeoye Adeniyi, F. P. Adler, Andani Andan, M. F. Anderson, W. C. Anoff, E. N. Armitage, P. M. Ashby, Susan M. Atherton, A. F. J. Atkins, B. N. Ballantine, R. B. Barrett, J. L. Beecher, Audrey J. Belsham, W. H. C. Berry, Margaret L. Birtwistle, R. G. Black, Shirley M. Blackman, P. D. Blade, A. R. H. Bliss, Sonia G. Bolton, Shirley A. Bond, David Booth, J. G. Bradbrooke, C. L. Bray, William Brown, M. D. Burgess, Evelyn M. J. Callis, B. J. Camp, H. M. Carpenter, I. P. Cast, B. Wan-Bun Chan, John Chapman, K. G. A. Clark, Jane M. Clegg, N. M. Cole, Heather J. Collins, Pauline T. Combe, Derek Corless, Dorothy K. Cory, J. C. Craggs, Jennifer Craig, Michael Culloty, J. C. Cummins, D. J. W. Darby, Margaret Davidson, Gareth Davies, Gillian M. Davies, P. B. M. Davis, R. S. Dawkins, A. D. Dean, J. M. Dinham, P. G. J. Dobson, I. S. Duff, Diana Dutton, J. D. Eddy, D. P. Edmunds, D. A. Edwards, R. W. England, A. W. G. English, P. R. Evans, C. B. Everett, Ann D. Fairclough, H. M. Fisher, D. J. Fishlock, R. A. Forster, J. V. Fowles, Joanna M. Fraser, Stanley Freedman, Gillian Freeman, Sebastian Freudenberg, Jill Fyfield, Gillian A. Garnett, J. A. Garrod, A. R. Geach, Penelope A. Gething, Sheila M. Girvan, W. A. Gould, Patricia A. Green, Patricia E. L. Greenlaw, J. L. Grogono, Pamela M. Haigh, Joyce C. Hall-Tomkin, Josephine E. Hammond, R. G. Harding, N. F. Harley, R. I. Harrison, J. C. Hasler, J. D. Hatch, I. B. Hayter, J. B. Hicks, G. T. Hollingworth, D. A. Hollis, Alison M. Holloway, P. T. Horder, A. S. Horniblow, E. R. Howard, D. P. M. Howells, David Hughes, G. V. Hughes, Janet E. Hughes, J. P. Hughes, M. S. Hughes, D. M. Hunter, Joanna E. Hunter, J. A. Hunter, Pamela J. Hunter, A. C. M. Inwald, R. M. Jeffery, K. A. Johansen, M. L. Jones, P. A. Jones, Winifred A. Kane, J. H. Kiff, A. W. Kilroy, David King, D. P. E. Kingsley, Kwamena Kyei-Mensah, T. R. Lawson, D. A. Lee, Sheila J. Lees, Thomas Lehner, Eveline B. McCulley, R. H. Mackeith, R. F. M. McKenzie, A. C. MacLean, D. R. Macnair, W. J. McNeilly, K. M. A. Madgwick, M. P. Madigan, E. J. B. Makin, Batu Malek, Elaine M. Maliphant, Eli Babajiya Mama, Deirdre H. Marlow, G. S. Martinez, Bridgett A. Mason, R. J. Mecoy, Joanna Merry, G. M. Michael, Felicity A. Milburn, M. H. Millward, R. D. G. Milner, C. A. L. Moon, John Moore, R. W. Morris, Ursula V. L. Morris, J. D. Morrison, C. W. Mortimer, P. B. Mudge, F. G. M. Musleh, J. F. O. A. I. Mustaffah, T. G. Nash, H. G. Naylor, M. I. M. Noble, J. R. Norman, Margaret A. Nunan, Ezekwe Ojinmah, C. N. Paine, Ann Parker, J. B. R. Parker, Rosemary C. Parrington, Sheila M. Pask, J. P. Patten, J. F. Pearson, John Pearson, Heather Pell, H. G. Peters, A. H. Pickering, D. A. Pocock, C. J. F. Pool, A. E. Pratt, R. B. Priscott, Edward Proctor, Vajri Promtatvethi, Yvonne F. Ransley, Jacqueline J. Rees, J. H. K. Reeves, D. S. Restall, R. S. Richardson, Anne P. Roberts, J. R. Robson, I. C. Roddick, P. J. Sanderson, Thomas Sherwood, Ann Simpson, I. P. Slee, D. H. Smith, Patrick Smith, P. H. Sönksen, C. J. Spivey, D. J. Stern, A. F. S. Stewart, H. J. S. Sudgen, D. R. Sutherland, D. J. M. Taylor, G. W. Thomas, W. H. Thomas, R. G. N. Thomson, Sheila M. Thwaites, Angela R. Till, Isobel Tomkins, F. D. Trevarthen, Wendell Tsao, P. L. H. Vernon, Harvey Wagman, C. J. S. Walter, G. G. Ward, R. J. Warner, P. H. Waterfield, A. V. Watkins, C. L. W. Webb, Diana V. A. Whitaker, M. M. Wicks, Wendy E. Williams, D. G. Willits, D. P. Winter, Margaret Woodford, Rosemary J. Wool, F. M. Young, Ting Chiu Yu.

Royal College of Surgeons in Ireland

On Nov. 17 the fellowship of the college was conferred on H. B. Devlin, D. G. Kelly, and W. J. Twibill.

College of General Practitioners

At the annual general meeting of the college on Nov. 19, Dr. Annis Gillie, chairman of council, said that more than 6000 members and associates had joined since its foundation—nearly 700 during the past year. There were now 35 faculties; 25 in the United Kingdom and Eire, 4 in New Zealand, 1 in Kenya, and 5 in South Africa where a South African Council of the college was soon to be formed. The special committee, under Sir Harry Jephcott, had raised £345,000 in a few months.

Dr. G. F. Abercrombie was re-elected president. Sir Harry Jephcott was appointed an honorary fellow. Dr. G. L. Hindson (Northumberland) was presented with the Butterworth gold medal for 1959–60.

General agreement was obtained to the proposed memorandum and articles of association of the new incorporated college.

At a meeting of the new council, held later, Dr. Annis Gillie was re-appointed chairman, Dr. K. M. Foster, vice-chairman, Dr. H. L. Glyn Hughes, hon. treasurer, and Dr. J. H. Hunt hon. secretary.

Dinner to Dr. W. N. Pickles

After the war the doctors of Wensleydale met several times at the home of Dr. Pickles in Aysgarth to discuss the proposed health service. Out of those meetings grew the annual doctors' party, usually held in late spring, to which each year Dr. Pickles invited a guest speaker. On Oct. 22, Dr. and Mrs. Pickles were themselves the guests of all those whom they had entertained at their spring parties. During the dinner, which was held at Leyburn, presentations were made to them both.

Clinical Aspects of Genetics

The Royal College of Physicians of London have chosen this subject as the theme of their next conference, which will be held on March 17 and 18. It is primarily arranged for fellows and members who are consultants in medicine or pathology.

The speakers will include Dr. J. A. Fraser Roberts, Dr. J. N. Walton, Dr. Eliot Slater, Dr. C. O. Carter, Dr. C. E. Ford, Prof. P. E. Polani, Dr. W. M. Court Brown, Prof. L. S. Penrose, Dr. Marco Fraccaro, Prof. C. E. Dent, Prof. Harry Harris, Dr. Charles Burnett, Dr. H. Lehmann, Dr. R. B. McConnell, Dr. R. T. C. Pratt, and Dr. C. A. Clarke. Numbers may have to be limited, and application should be made to the Registrar at the College, Pall Mall East, S.W.1, not later than Jan. 23. The entrance fee is five guineas, which should *not* be sent with the application.

Congress of the International Diabetes Federation

This congress will be held in Geneva from July 10 to 14. Particulars may be had from the secretary general of the congress Dr. Bernard Rilliet, 4, boulevard des Tranchées, Geneva, Switzerland.

International Federation of Gynæcology and Obstetrics

A world congress of this Federation will be held from Sept. 3 to 9 in Vienna. Further particulars may be had from the scientific secretary of the Federation, Dr. V. Grünberger, Alserstrasse 4, Vienna IX, Austria.

Quaker Medical Society

On Wednesday, Nov. 30, at 8.30 P.M., at Friends House, Euston Road, London, N.W.1, Dr. Cuthbert Dukes will give a Lister lecture. His subject will be Dr. John Fothergill (1712–1780) and his Medical Contemporaries.

Proctologica Latina Collegium

An international meeting of colon and anorectal surgery is to be held by this body from May 18 to 20 in Tangier. Further particulars may be had from the general secretary of the collegium, Dr. G. B. E. Simonetti, 3, via S. Raffaele, Milan, Italy.

International Congress for Microbiology

This congress will be held at Montreal, from Aug. 19 to 25, 1962. There will be five sections—structure and function, agricultural microbiology, industrial microbiology, medical and veterinary microbiology, and virology. Inquiries should be sent to Dr. N. E. Gibbons, National Research Council, Ottawa 2, Canada.

Richard Kovacs Prize

The first award of this prize has been made by the Royal Society of Medicine to Dr. Philippe Bauwens. Dr. Bauwens will receive the prize and deliver a lecture on May 10.

The prize, which has been established by Mrs. Ina Kovacs in memory of her husband, the late Dr. Richard Kovacs, is to be awarded triennially for work in physical medicine.

British Diabetic Association

On Oct. 14–15 the medical and scientific section of this Association met in Glasgow. The first day was devoted to a colloquium on prediabetes, including 14 papers. One suggestion made was a trial of the syuphonylureas in human prediabetes, and the committee of the section is now planning such a trial. On the second day there was a paper and discussion on the care of elderly diabetics, followed by 7 further papers. The meeting was well attended, and Dr. Jørgen Pedersen, of Copenhagen, was a guest speaker.

Anglo-French Exchange Bursaries

Applications are invited for bursaries to be awarded in 1961 to young British doctors under the exchange scheme arranged by the French Embassy in London between the Institut National d'Hygiène in Paris and the Ciba Foundation in London.

The grants (870 francs a month) will be awarded for two to four months to medical men who wish to obtain clinical experience or carry out research in France. Application forms may be had from the director of the Ciba Foundation, 41, Portland Place, London, W.1. The closing date for applications is Jan. 31.

Ministry of Health

Dr. N. M. Goodman has been appointed a deputy chief medical officer of the Ministry.

Dr. Goodman was educated at Mill Hill and went from Sandhurst to the Worcestershire Regiment, with which he served in France, Belgium, and Germany. Demobilised with the rank of captain, he went to Pembroke College, Cambridge, and the London Hospital, and after qualifying in 1923 spent eight years in general practice. In 1934, after taking the D.P.H., he joined the staff of the Ministry of Health. From 1937 to 1944 he was the British delegate on the Permanent Committee of the Office International d'Hygiène publique and a member of the health committee of the League of Nations. In 1945 he was appointed deputy director of Health for Europe for UNRRA. Two years later he became director of field services of W.H.O., and in 1948 assistant director-general of W.H.O. In 1949 he rejoined the staff of the Ministry. In 1955 he became the principal medical officer particularly concerned with the hospital and local-authority services of the four Metropolitan regions. Dr. Goodman has been on official missions to most of the countries in Europe, and to U.S.A. and Ethiopia, and was the Arris and Gale lecturer at the Royal College of Surgeons in 1944. He was elected F.R.C.P. in 1950. His book on *International Health Organisations and their Work* was published in 1952.

Association for the Study of Medical Education

The function and structure of the teaching hospital has been chosen as the theme of the conference which the Association is holding at the Royal College of Physicians of London, Pall Mall East, S.W.1, on Dec. 2 at 10 A.M. Sir Robert Platt, P.R.C.P., will be in the chair, and Sir Russell Brain will open the conference.

Mr. P. H. Jayes has been appointed civil consultant in plastic surgery to the Royal Air Force.

On Saturday, Dec. 10, at 2.30 P.M., at Mapperley Hospital, Nottingham, the Sheffield Regional Psychiatric Association is to hold its inaugural meeting, when Prof. E. Stengel will speak on relationships between psychiatric classification, nomenclature, and diagnosis.

Dr. G. Georgieff, of the Ethiopian Government Ministry of Health Anti-Epidemic Service, is appealing for 1959 issues of *The Lancet*. Any reader who is able to help is asked to get in touch with Dr Julius S. Prince, P.O. Box 1035, Addis Ababa, Ethiopia.

At a meeting of the Medical Electronics Discussion Group on Friday, Dec. 2, at 6 P.M., at the Institute of Electrical Engineers, Savoy Place, London, W.C.2, there will be a discussion on telemetering biological data. The opening speakers will be Dr. G. H. Byford and Dr. K. G. Williams.

A semipermanent exhibition will be held at the Institute of Dermatology, Lisle Street, London, W.C.2, from Dec. 1 to 27, by Dr. B. E. D. Cooke on bullous lesions affecting the oral mucosa.

The Scientific Film Association (3, Belgrave Square, London, S.W.1) is revising its records of medical films for a new edition of its guide, and would be pleased to receive details of any films not previously included.

A Supplement 1957–1959 to H. K. Lewis's Medical, Scientific and Technical Library Catalogue is now available from P.O. Box 66, 136, Gower Street, W.C.1; price to subscribers 5*s*., to others 10*s*. 6*d*.

Births, Marriages, Deaths

BIRTH

JACKSON.—On Nov. 14, at Central Middlesex Hospital, to Eileen (née Greenwood), wife of John W. Jackson, F.R.C.S., a daughter—Jane Elizabeth—a sister for Jennifer and Adam.

DEATHS

PHILLIPS.—On Nov. 19, at the Duke of York Home, Bradford James Phillips, F.R.C.S., J.P., aged 86 years, of 4, Marlborough Road, Bradford, 8, the very dearly loved husband of Rose Phillips and dear father of Jean. Cremated at Nab Wood Crematorium, Shipley, on Nov. 23.

RATHBONE.—On Nov. 15, following a stroke, Mary (May) Rathbone, L.M.S.S.A., F.L.S., of The Poplars, Westington, Chipping Campden, daughter of the late Theodore Rathbone, J.P., of Backwood, Neston, Cheshire, in her 94th year.

Diary of the Week

NOV. 27 TO DEC. 3

Monday, 28th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. J. S. Robson: Renal Excretion of Water in Health and Disease.
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4.30 P.M. (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Mr. A. L. T. Easton: Surgical Complications of Pregnancy.
MANCHESTER MEDICAL SOCIETY
9 P.M. (Medical School, University of Manchester.) *General Practice.* Prof. R. E. Lane: Doctor in Industry.

Tuesday, 29th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
5 P.M. Dr. K. D. Keele: Evolution of Clinical Methods in Medicine. (First of two FitzPatrick lectures.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. H. B. Stallard: Malignant Melanoma of the Choroid Treated with Radioactive Applicators.
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. L. E. Glynn: Auto Antibodies and Diseases of Connective Tissue.
INSTITUTE OF CHILD HEALTH, THE HOSPITAL FOR SICK CHILDREN, Great Ormond Street, W.C.1
5.30 P.M. Dr. G. A. Neligan: Physiological Measurements in Newborn Infants.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. C. D. Calnan: Cutaneous Allergy.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. (Wright-Fleming Institute.) Mr. Philip Rhodes: Fluid Balance in Obstetrics.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Dr. G. F. Swann: Myelography.
ROYAL STATISTICAL SOCIETY
5.30 P.M. (London School of Hygiene and Tropical Medicine.) *Medical Section.* Dr. J. M. Tanner: Biometrical Problems in Studies of Human Growth.
LEEDS NEUROLOGICAL SCIENCES COLLOQUIUM
5.15 P.M. (General Infirmary at Leeds.) Sir Aubrey Lewis: Evaluating Psychiatric Treatment.

Wednesday, 30th

UNIVERSITY OF LONDON
5.30 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Dr. J. J. Bunim (Bethesda): Interrelationship of Collagen Diseases.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. Victor Wynn: Electrolyte Metabolism.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Cellular Nævi and Malignant Melanomata.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. Howard Nicholson: Diffuse Interstitial Pulmonary Fibrosis.
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
2 P.M. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Dr. Robert Newton: Pouch of Douglas.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. J. P. Bull: Problem of Domestic Burning Accidents.
MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) Dr. M. I. Grossman: Gastro-œsophageal Reflux.

Thursday, 1st

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P.M. Dr. K. D. Keele: Evolution of Clinical Methods in Medicine. (Second of two FitzPatrick lectures.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.30 P.M. Mr. J. B. Pennybacker: Acoustic Neuroma.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Neurology.* Mr. F. J. Gillingham, Mr. Ian McCaul, Mr. John Hankinson: Stereotaxic Surgery in Neurological Disease.
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Bernard Lennox: Nuclear Sexing and Human Chromosomal Anomalies.
ST. MARY'S HOSPITAL MEDICAL SCHOOL
5 P.M. (Wright-Fleming Institute.) Prof. R. W. Scarff: Proliferative Lesions of the Breast. (Kettle lecture.)
NUFFIELD ORTHOPÆDIC CENTRE, WINGFIELD-MORRIS ORTHOPÆDIC HOSPITAL, OXFORD
8.30 P.M. Mr. Geoffrey Platt: Arthroplasty of the Knee.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Sir Eric Riches: Carcinoma of the Bladder.

Friday, 2nd

ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Otology.* Mr. Pennybacker, Mr. J. D. K. Dawes: Intracranial Complications of Otogenic Origin.
2.30 P.M. *Laryngology.* Prof. R. S. Illingworth, Mr. René Thomas, Dr. W. J. E. McKee: Is Removal of Tonsils and Adenoids Necessary?
5.30 P.M. *Anæsthetics.* Prof. R. F. Woolmer: Information Please. (Presidential address.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. A. P. Forrest: Hypophysectomy in the Management of Patients with Malignant Disease.
4 P.M. Prof. G. A. Smart: Spectrum of Thyroiditis.
SOCIETY OF APOTHECARIES OF LONDON, Black Friars Lane, E.C.4
5.30 P.M. *Medicine and Pharmacy.* Dr. A. H. T. Robb-Smith: Growth of Knowledge of Function of Blood.
HEBERDEN SOCIETY
4.15 P.M. (Wellcome Foundation, Euston Road, N.W.1.) Dr. Bunim: Broadened Spectrum of Sjögren's Syndrome and its Pathogenetic Implications. (Heberden oration.)

Saturday 3rd

MIDLAND THORACIC SOCIETY
3 P.M. (Birmingham Medical Institute, 36, Harborne Road, Birmingham, 15.) Dr. D. A. Heath: Hypertensive Pulmonary Vascular Disease.